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DIAGNOSIS AND CLINICAL MANAGEMENT OF FUNCTIONING CARCINOIDS

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Functioning carcinoid is a serotonin-secreting argentaffin tumor which may metastasize. The excess serotonin produces special symptoms, such as characteristic spells of flushing of the skin, and is associated with the appearance of abnormal amounts of 5-hydroxy-3-indole acetic acid in the urine. In addition, the functioning carcinoid may induce cramps, diarrhea, and other less typical symptoms generally associated with intra-abdominal tumors. Histories of 12 patients with this disease are given in detail. The primary lesion was located in the small intestine in seven patients. The diagnosis is confirmed by the finding of abnormal quantities of 5-hydroxy-3-indole acetic acid in the urine. The best current treatment is surgical removal of as much of the tumor as possible.

TRACING the development of the syndrome known today in the United States as functioning carcinoid and abroad as metastasizing argentaffin carcinoma is like watching the pieces of a giant jigsaw puzzle fall together. After the description of carcinoids as a pathological entity, it was originally thought that these were benign lesions. However, around the turn of the century it became apparent that they may metastasize and produce masses in the abdomen. Not until five years ago was it realized that they function as endocrine tumors in the sense that they secrete serotonin, which exerts its effects on the vessels of the skin, the smooth muscle of the gastrointestinal tract and bronchi, and the valves of the heart and is found also in the brain, where its function is under study. We ordinarily think of an endocrine tumor as acting through its hormones, in the classic fashion, but resulting in overstimulation of a normal physiological process; for example, the production of hypoglycemia by an islet cell adenoma of the pancreas. However, in the syn-

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drome of functioning carcinoid there is no known normal parallel, and the clinical picture produced is entirely pathological.

The primary carcinoid lesion is usually very small, may often be multicentric, and frequently is situated in the distal part of the ileum, but metastatic lesions may occur after many years, grow slowly, and assume massive proportions. Metastasis usually occurs to the lymph nodes and liver, and occasionally to the lungs, bones, and ovaries. It is generally agreed that carcinoids, especially those arising in the stomach, small intestine, and colon, are malignant and may metastasize. Pathologists [1] estimate that carcinoids arising in the appendix constitute from 58 to 90% of all carcinoids. Extra-appendiceal lesions may arise in the stomach, duodenum, jejunum, ileum, cecum, colon, rectum, gallbladder, gastrointestinal components of a teratoma, and, as recently observed, in the lungs. It is stated that appendiceal carcinoids are of an unusually low grade of invasiveness, and in a review of the English language literature and in his series of 207 appendiceal carcinoids MacDonald [15] could find no adequately documented instance of metastasis beyond regional lymph nodes.

After acceptance of the concept that carcinoids are malignant and may metastasize, little new information was added until a peculiar syndrome, that of functioning carcinoid, was described by Biörck and co-workers [2] in 1952 and by Thorson and co-workers [3] in 1954. They gave criteria for diagnosis and expressed the view that metastasis to the liver is an important factor in the genesis of this syndrome and that the common denominator in the production of its signs and symptoms is 5-hydroxytryptamine, or serotonin.

Investigations on Carcinoids and Serotonin

Many investigators have studied the pharmacological aspects of this substance and its relationship to this syndrome. Erspamer,[4] in the mid 1930's and early 1940's, conducted investigations leading to the identification of enteramine, a substance imparting peculiar histochemical properties to the enterochromaffin cells of the gastrointestinal mucosa. Rapport and co-workers,[5] in 1948, isolated from beef serum a crystalline vasoconstrictor substance which they called serotonin. The next year Rapport [6] proposed the constitutional formula of 5-hydroxytryptamine for this substance. Hamlin and Fischer [7] confirmed this structure by synthesis of serotonin in 1951. A year later Erspamer and Asero [8] identified enteramine as 5-hydroxytryptamine and also synthesized it. In 1953, Lembeck [9] extracted 5-hydroxytryptamine from a carcinoid found at autopsy and thus corroborated Erspamer and Asero's assumption of the origin of the substance.

Page and McCubbin,[10] Comroe and associates,[11] Gaddum,[12] and others have studied relationships between the clinical syndrome of functioning carcinoid and the pharmacological action of 5-hydroxytryptamine. In 1955, Erspamer [13] discussed the degradation of 5-hydroxytryptamine to 5-hydroxy-3-indole acetic acid, Page and associates [14] and Sjoerdsma and Udenfriend [15] demonstrated an increase of the latter substance in the urine of patients with carcinoids, and Sjoerdsma and associates [16] described a simple test for the diagnosis of metastatic carcinoid. Udenfriend and associates [17] presented a method for quantitative assay of 5-hydroxy-3-indole acetic acid in normal urine soon thereafter. At about this time, Pernow and Waldenström [18] and Page and associates [14] expressed their reasons for considering argentaffin carcinoma or functioning carcinoid as an endocrine tumor. They expressed the view that the whole syndrome results from increased production of a pharmacologically active substance by the malignant cells and stated that the presence of large amounts of 5-hydroxy-3-indole acetic acid in the urine may be regarded as the best indication of the presence of functioning carcinoid.

Further understanding of the syndrome was advanced by the reports of Sjoerdsma and associates [19] when, using tryptophan labeled with radioactive carbon (C^{14}), they were able to demonstrate the pathway for the production of 5-hydroxytryptamine and its ultimate breakdown to 5-hydroxy-3-indole acetic acid. MacDonald,[15] in 1956, studied data on 356 carcinoids of the gastrointestinal tract gathered from the records of the Boston hospitals and added four new cases of the syndrome of functioning carcinoid. He said that the addition of his new cases brought the total number of acceptable cases of this syndrome reported to that time to 57. In this report he documented the pathological findings in regard to the valvular lesions of the right side of the heart. He also noted a rather high incidence of gastric and duodenal ulcer in association with carcinoids. He suggested, too, that some relationship might exist between these tumors and arthritic changes usually involving the joints of the fingers. Several other cases of this syndrome have been reported since MacDonald's review, including four cases that we presented [20] in May, 1957, at the meeting of the American Gastroenterological Association.

In the past year and a half principal interest has centered about the relationship of serotonin and its precursor, 5-hydroxytryptophan, to the production and excretion of histamine in patients with this syndrome. Large amounts of histamine have been demonstrated in the urine obtained from these patients, and blood studies [21] have shown high levels of 5-hydroxytryptophan. It was also demonstrated [22] that the tumor pool of serotonin could be calculated by using radioactive labeled 5-hydroxytryptophan. Recently it has been postulated that a tumor exists which secretes 5-hydroxytryptophan, produces an atypical picture of functioning carci-

noid,[23] and is characterized by the excretion of large amounts of histamine as well as large amounts of 5-hydroxytryptophan and serotonin in the urine, but has only small amounts of serotonin present in the tumor.

A very extensive review of the physiological properties of serotonin as described during the last four years has been presented recently by Page.[24] The popularity of this subject currently is attested to by the fact that Page listed 529 references in this review article. The reader is referred to this excellent article for a comprehensive survey of this interesting substance and the many interesting and important studies in relation to this substance and functioning carcinoid.

Report of Cases

CASE 1.—A 72-year-old woman was admitted to the Mayo Clinic in March, 1957, with the complaint of loss of weight during the last seven months. For 50 years she had had right subcostal aching, bloating, and gaseous distention with occasional pain extending through to the back. For four years she had tired easily. For three years she had had a stinging sensation on the right side of the tongue. For two years episodes of flushing of the face had occurred on the average of once or twice a week. The flush began at the back of the neck, spread over the neck and face, and involved the upper anterior part of the thorax. The flush appeared to be irregular or spotty on the neck, but was diffuse over the face. She felt hot during the flush, and her husband stated that she "looked as red as fire." The flush lasted for a few minutes and seemed to be precipitated by eating, usually occurring 10 minutes after meals. She denied diarrhea, asthma, or cardiac symptoms. For nine months she had been aware of recurrent, severe cramping epigastric pain which was worse after meals and occasionally awakened her at night. Relief was obtained by vomiting or belching. In the three months prior to admission she had fainted three times. She had reduced her intake of food because of pain and had lost 23 lb. (10.4 kg.).

The patient weighed 97 lb. (44 kg.). The blood pressure, pulse, and temperature were normal. There were no cardiac murmurs and no palpable abdominal masses or organs. Studies of the blood and urine disclosed only mild hypochromic anemia. Urinalysis was positive for 5-hydroxy-3-indole acetic acid. X-ray examination of the thorax, gallbladder, and stomach did not reveal any abnormality. Proctoscopic examination gave negative results. On March 25, 1957, abdominal exploration disclosed in the upper part of the ileum a carcinoid 1.2 cm. in diameter. There was extension to the root of the mesentery with involvement and obstruction of the superior mesenteric vein by a mass measuring 5 to 6 cm. Biopsy proved the diagnosis of carcinoid. Four or five metastatic nodules were found in the right lobe of the liver. Enteroenterostomy was done to relieve obstruction. The postoperative course was satisfactory. The administration of tryptophan seemed to increase the urinary excretion of 5-hydroxy-3-indole acetic acid (table 1).

CASE 2.—A 68-year-old woman came to the clinic on July 26, 1957, because of multiple enterocutaneous and colocutaneous fistulas. She gave a history of gaseous discomfort in the lower part of the abdomen, especially after eating a large meal in the evening. From 1950 to 1954 she had had four episodes of intermittent, incomplete obstruction of the small intestine. In 1954 she experienced episodes characterized by a red, blotchy flush involving the upper part of the trunk, the face, and the arms and associated with extreme sweating of the neck and face. The episodes lasted five minutes, seemed to be precipitated by alcoholic beverages, emotional upsets, and occasionally by eating and had gradually progressed in severity and frequency.

In March, 1957, abdominal exploration elsewhere disclosed hepatic metastatic lesions and the abdomen was closed. Postoperatively, x-ray studies revealed an obstructing lesion in the ileum. On May 21, she was again operated on elsewhere to relieve intestinal obstruction. She had a stormy postoperative course and seven days later underwent reexploration of the abdomen because of multiple enterocutaneous and colocutaneous fistulas. On June 28, an unsuccessful attempt was made elsewhere to close the fistulas. Her clinical condition continued to decline, the severity of the flushing and sweating episodes increased, and her mental condition deteriorated.

When she was transferred to the clinic on July 26, examination disclosed emaciation, debilitation, dehydration, and confusion. She was perspiring profusely over the head, face, and neck. She had no heart murmurs. There were several abdominal fistulas. Marked excoriation of the skin of the abdominal wall was present from intestinal drainage. Palpation of the abdomen was difficult, but no gross masses could be felt. At admission she had leukocytosis and marked electrolyte imbalance. Quantitative analysis of 1,290 cc. of urine (a 24-hour specimen) yielded 16.9 mg. of 5-hydroxy-3-indole acetic acid. Fluid and electrolyte imbalance was corrected, with progressive improvement in the patient's general condition. The infected abdominal skin cleared after adequate treatment. Surgical closure of the fistulas was advised, but the patient declined closure and requested dismissal.

TABLE 1—*Effect of Certain Drugs on Urinary Content of 5-Hydroxy-3-Indole Acetic Acid*

Date, 1957	Urine, Cc.	5HIAA, Mg./24 Hr.	Drug Used
		Case 1	
3/30	1,830	24.9	...
4/ 1	1,150	13.1	...
4/ 2	570	5.4	...
4/ 5	...	...	Tryptophan, 1 Gm.
4/ 6	630	19.5	...
4/ 7	521	16.2	...
		Case 3	
10/23	...	25.2	...
10/24	...	29.0	...
10/26	...	...	Tryptophan, 3 Gm.
10/27	1,200	50.0	...
10/28	1,070	39.0	...
10/29	1,030	41.0	...
10/30	...	32.0	Hydroxyzine hydrochloride, 25 mg., q.i.d.
10/31	...	22.0	Hydroxyzine hydrochloride, 25 mg., q.i.d.
		Case 8	
6/12	775	41.0	...
8/22	...	...	Tryptophan, 2 Gm.
8/23	1,130	92.0	...
9/ 3	...	52.0	Reserpine, 0.25 mg., q.i.d.
9/ 4	...	37.0	Reserpine, 0.25 mg., q.i.d.

CASE 3.—This patient was initially seen at the clinic in May, 1940, at age 43 for repair of a postpartum rectovaginal fistula. She was next seen in March, 1941, at which time diagnoses of adenomatous goiter without hyperthyroidism and psychoneurosis were made. On a return visit early in 1943 the same diagnoses were made. Later, in April, 1953, she returned because of symptomatic gallstones. Cholecystectomy was performed. At operation the surgeon observed that appendectomy and hysterectomy had been performed previously. There were dense adhesions in the right lower quadrant of the abdomen. Pathological examination of the gallbladder disclosed chronic cholecystitis with moderately thickened and infiltrated walls. Gallstones were present.

The patient was next seen in October, 1957, when she was 60 years old. Since August, 1955, she had had diarrhea characterized by 8 to 15 watery stools in 24 hours. In the spring of 1957, cramping pain had developed in the lower part of the abdomen. Her home physician found a lesion in the cecal region on x-ray examination and advised operation. In August right hemicolectomy and ileocolostomy were performed elsewhere. A diagnosis of carcinoid was made. The surgeon stated that there was a mass in the terminal part of the ileum with involvement of the lymph nodes up to the base of the mesentery and up either side of the aorta. After operation the diarrhea persisted, although the cramping was relieved.

The patient soon experienced episodes of flushing, having had 12 in the two-month period between operation and observation at the Mayo Clinic. She said that the flush occurred over the head, neck, shoulders, thorax, and upper part of the arms and that the skin became deep red "like a lobster," the skin felt as if it were burning. There was no associated sweating. The episodes usually lasted five minutes but one had lasted an hour. They had awakened her from sleep at night. She knew of no precipitating factors. She said that palpitation and dyspnea were associated with the flush and that the episodes were definitely different from those she associated with menopausal "hot flushes." She had not had asthma. She had lost 28 lb. (12.7 kg.) since operation.

When she was examined at the clinic in October, 1957, her blood pressure was 135 mm. Hg systolic and 90 diastolic, and temperature was 99.2 F (37 C). She was thin, nervous, and tense. A small adenomatous goiter was present. There were multiple abdominal scars, the most recent one being reddened and tender. The edge of the liver was palpable 3 cm. below the costal margin on deep inspiration and was firm. A mass measuring 4 by 6 in. was present in the right lower quadrant. This mass was firm and nontender, and massage did not produce a flush. There were no cardiac murmurs.

Laboratory studies disclosed mild hypochromic anemia, normal serum bilirubin level, normal excretion of sulfobromophthalein, and normal prothrombin time. The results of proctoscopic examination were negative. X-ray examination showed that resection of the cecum had been performed and that an end-to-end ileocolonic stoma was functioning freely. The results of examination were otherwise negative. The x-ray appearance of the thorax was normal. Urinalysis on two occasions yielded 25.2 mg. and 29 mg. of 5-hydroxy-3-indole acetic acid in 24-hour specimens of urine.

Urinary excretion of 5-hydroxy-3-indole acetic acid after administration of tryptophan and various drugs was studied (table 1). Then abdominal exploration was carried out. Many small metastatic implants were found in the liver. Also, tumor-containing nodes occupied the root of the mesentery of the small intestine, and these were not resectable. Forty milligrams of a specimen of tissue removed for biopsy and determination of the serotonin content gave a positive reaction for serotonin. Postoperative recovery was uneventful. Diarrhea and flushing were unaffected by hydroxyzine hydrochloride therapy. In January, 1958, the patient stated that her appetite was good and that the diarrhea was less severe. She had gained slightly in weight. Flushes were severe, occurring daily and now involving the entire body. After a flush she felt exhausted and depressed. She was taking chlorpromazine, 25 mg. four to six times a day. She was advised to increase this dosage.

Case 4.—A woman aged 54 who came to the clinic in January, 1958, said that for the past 10 years she had had occasional episodes of hot flushes and sweating. These would occur as often as three times a day for two to seven days and then would not occur for weeks at a time. During the last year the flushes had become more frequent, had occurred several times daily, and had lasted two minutes or more. The episodes would come and go, apparently unrelated to ingestion of food or activity. She stated that during a flush the face, neck, arms, forearms, and thorax would be involved with a florid red, blotchy rash. For the past five months she had noted fulness in the upper part of the abdomen and she had seemed to become full easily with meals. For two months she had diarrhea characterized by 10 to 12 liquid, yellow to green bowel movements per 24 hours. She had lost 30 lb. (13.6 kg.) and appeared slender and tense.

During the examination she flushed several times at intervals of three to five minutes, and each flush lasted for 30 to 60 seconds. During the flush there were diffuse redness and patches of blotchy erythema over the face, neck, upper anterior and posterior parts of the thorax, breasts, arms, forearms, and abdomen. The liver was massively enlarged, hard, coarsely nodular and easily palpable down to the right iliac crest and across the abdomen to the left upper quadrant. The spleen could be palpated 4 cm. below the left costal margin. There was a systolic pulmonic murmur. Massage of the liver produced a flush, as did pelvic and rectal examination. Other than a sulfobromophthalein retention of 10% at the end of one hour, results of studies of the blood and urine were not remarkable. X-ray examination of the thorax showed an elevation of the diaphragm on the right. A plain roentgenogram showed a soft-tissue mass in the upper part of the abdomen, mostly on the right. A 24-hour specimen of urine yielded 11.4 mg. of 5-hydroxy-3-indole acetic acid. The patient was advised of the tentative diagnosis, and further studies were suggested, but she elected to return home without further study.

Case 5.—A 53-year-old woman came to the clinic in January, 1958, with the complaint of chronic cough of 15 years' duration, which had been worse in the past year. Five months before admission she had begun to have hemoptysis which persisted and became a daily occurrence. She had febrile episodes during this period. She wheezed frequently with respiration. For two months she had had substernal distress precipitated by paroxysms of coughing. She was dyspneic after rapidly walking half a block. The blood pressure was 166/96 mm. Hg. There was no cardiac murmur. She denied diarrhea or flushing. The liver was palpable two fingerbreadths beneath the right costal margin.

Studies of the blood and urine gave negative results. Studies of 5-hydroxy-3-indole acetic acid were not done. X-ray examination of the thorax revealed calcification and torsion of the aorta. Cytological examination and culture of the sputum and examination for acid-fast organisms gave negative results. Bronchoscopic examination disclosed a bleeding lesion in the left lower-lobe bronchus; at biopsy this proved to be a bronchial adenoma of the carcinoid type. At left pneumonectomy a high grade 1 adenocarcinoma of the carcinoid type measuring 5 by 3 by 4 cm. was encountered arising in the left lower-lobe bronchus 3.5 cm. below the level of transection of the main bronchus. The tumor had penetrated deeply and eroded into the upper-lobe bronchus. Several nodes immediately adjacent to the tumor were metastatically involved. Hilar nodes were inflamed. The tumor contained 31 mcg. of serotonin per gram.

Case 6.—A 63-year-old woman came to the clinic in February, 1958, with the complaint of a productive cough of two and one-half years' duration. She had been seen here previously, in September, 1951, because of asthma and pneumonitis involving the left base. She had returned in February, 1952, at which time it was found that rheumatoid arthritis had developed in the interval. In September, 1955, she was seen because of rheumatoid arthritis and pulmonary nodules which were thought to be granulomas in the left base.

At the present time the asthma continued unchanged. She denied diarrhea or flushing of the skin. Her home physician had found new nodules on the right side in the course of x-ray examination of the thorax and had referred her for evaluation of her condition.

The patient weighed 161 lb. (73 kg.). Her thought and speech appeared somewhat slowed. Her blood pressure was 150/80 mm. Hg. There were sticky rales at each base posteriorly. The changes of rheumatoid arthritis were evident in the fingers of both hands. The erythrocyte sedimentation rate was 72 mm. per hour (Westergren method). Urinalysis gave negative results. Studies for 5-hydroxy-3-indole acetic acid were not done. X-ray examination showed three masses in the middle lobe of the right lung, and the question was raised as to the presence of small nodules in both pulmonary fields which might be metastatic. At thoracotomy the large circumscribed lesion seen on x-ray examination was found to be in the fissure between the right middle and the right upper lobe. There were also multiple small nodules in the right middle and lower lobes, and consequently these lobes were removed.

The surgical pathologist reported carcinoid with multiple nodules throughout the lung but primarily in the periphery; the largest measured 3 by 2 by 2 cm. and the smallest 0.3 cm. in diameter. The larger tumor contained 86 mcg. of serotonin per gram of tumor, and the smaller tumor contained 62 mcg. per gram. Postoperative urinalysis for 5-hydroxy-3-indole acetic acid gave negative results. The postoperative course was satisfactory until the seventh day when tachycardia, shock, and gastric retention developed, and the patient died in spite of supportive treatment including administration of fluids, electrolytes, steroids, and levarterenol (Levophed) bitartrate.

At autopsy multiple benign adenomas were seen in the remaining right upper lobe. A hepatoma but no metastatic carcinoid nodule was present in the liver. Careful search of the entire gastrointestinal tract did not disclose any carcinoid lesion. There was no evidence of cardiac changes similar to those previously described[18] in the cusps of the valves of the right side of the heart. There was thrombosis of the portal vein.

Case 7.—This case is reported in detail elsewhere.[23] The patient was admitted to the hospital in October, 1957, because of severe pain and a mass just below the right inguinal ligament and superficial to the right femoral artery. Elsewhere she had undergone subtotal hysterectomy and appendectomy in 1943 and right pneumonectomy for a bronchial adenoma with metastasis to the hilar nodes in January, 1956. The bronchial lesion was of the carcinoid type. She had had recurrent pain in the right upper quadrant since April, 1957, and intermittent diarrhea and flushing episodes since July. The flushes occurred several times a week, involved principally the head, neck, and face, and lasted for periods ranging from 20 or 30 minutes to eight hours. A burning sensation of the face was associated with the flush. Her surgeon wrote that the results of urinalysis for 5-hydroxy-3-indole acetic acid were positive in the fall of 1957.

Physical examination disclosed the following findings: flushing and evidence of acute pain; blood pressure 110/60 mm. Hg; pulse 100; temperature 100 F (37.8 C); right pulmonary space surgically obliterated; no significant heart murmurs; enlarged, hard, coarsely nodular liver; large mass in the region of the gallbladder; a right femoral hernial sac measuring 1.5 by 1.0 cm., which disappeared while it was being examined; negative rectal findings; and absence of edema of the extremities.

Laboratory studies revealed hypochromic anemia; normal urine; retention of sulfobromophthalein, 18%; serum alkaline phosphatase level, 17.7 King-Armstrong units; rate of sedimentation of erythrocytes, 60 mm. per hour (Westergren method); and the presence of 5-hydroxy-3-indole acetic acid in the urine. X-ray examination disclosed that pneumonectomy had been performed on the right and that the left lung was clear. The gallbladder was nonfunctioning, according to x-ray evidence, and it contained stones. The referring physician kindly loaned sections of previously resected tissues which were reviewed by Dr. M. B. Dockerty, who reported evidence of chronic cervicitis, fibrosis of the uterus, and chronic fibrous appendicitis with no evidence of carcinoid from the organs removed in 1943; a primary bronchial adenoma of the carcinoid type was present in the specimen obtained at pneumonectomy in 1956.

Abdominal exploration on Nov. 4, 1957, disclosed a markedly enlarged liver with massive amounts of metastatic tumor tissue. One mass just above the inferior margin of the liver measured 8 cm. in diameter and was fluctuant but was distinctly not the gallbladder. A smaller superficial nodule was removed for biopsy. It was elected not to aspirate the large fluctuant mass. Inspection of the entire small intestine, cecum, and a portion of the transverse colon did not reveal any primary lesion or mesenteric nodal metastasis. The nodule removed from the liver was found to be metastatic grade 1 adenocarcinoma, carcinoid type.

Postoperative recovery was satisfactory. Flushing was temporarily relieved by the administration of chlorpromazine but became bothersome again after the patient was dismissed from the hospital.

Case 8.—A middle-aged man, who was initially seen at the clinic in June, 1957, gave the history that in September, 1945, 30 in. of the small intestine had been removed because of Meckel's diverticulum and carcinoid with obstruction and metastasis to lymph nodes. Six months later he began to have episodes of low abdominal crampy pain with the characteristics of intermittent, incomplete obstruction of the small intestine. Over ensuing years the episodes became more frequent and of longer duration until they precipitated his admission to the clinic. He denied flushing, asthma, swelling, or symptoms of impaired cardiac reserve. The only diarrhea he had experienced had occurred as episodes of partial obstruction subsided, at which time he would have two or three loose, watery movements during 24 hours, and then he would be entirely free from diarrhea until the next episode of incomplete obstruction.

Examination revealed blood pressure 122/80 mm. Hg; no heart murmurs; tenderness in the right lower quadrant of the abdomen; liver not palpable; no peripheral edema; no flushing; complete blood cell count normal; urine normal; liver function normal; x-ray appearance of the entire gastrointestinal tract normal; proctoscopic findings normal; absence of parasites and ova in the stools; and 41 mg. of 5-hydroxy-3-indole acetic acid in a 24-hour volume (775 cc.) of urine.

Exploration was advised, but the patient elected to defer this procedure. He returned in August, 1957. After oral administration of 3 Gm. of tryptophan, a 24-hour specimen of urine (1,130 cc.) on Aug. 23 yielded 92 mg. of 5-hydroxy-3-indole acetic acid (table 1). Exploration the next day disclosed recurrent and metastatic carcinoid of the ileum. Nodules were present in the liver. The terminal portion of the ileum, including the tumor, and the right side of the colon were resected, and ileotransverse colostomy was performed. The tumor tissue contained 545 mcg. of serotonin per gram. Postoperatively the urine continued to contain 5-hydroxy-3-indole acetic acid. After administration of 0.25 mg. of reserpine four times a day the urine contained 52 mg. of this substance on Sept. 3 and 37 mg. on Sept. 4. The patient continued to be entirely free of any symptoms of functioning carcinoid.

Cases 9, 10, 11, and 12 have been reported elsewhere.[20]

Clinical Features

According to the criteria described by Thorson and co-workers[9] and confirming observations by many authors, cardinal symptoms or findings include the flushing phenomenon, diarrhea, history of episodes of asthma, enlargement of the liver, dependent edema, and auscultatory findings compatible with pulmonic stenosis or tricuspid insufficiency

or both. Not all these features need be present simultaneously. In addition, abnormal amounts of 5-hydroxy-3-indole acetic acid should be demonstrable in the urine, and, if facilities are available, abnormal amounts of 5-hydroxytryptamine can be demonstrated in the blood or in tumor tissue. Needle biopsy of the liver may yield evidence of metastatic carcinoid tissue.

On the basis of the 12 patients (table 2) represented in this report the following information seems pertinent to diagnosis.

History.—A history compatible with previous episodes of intermittent incomplete obstruction of the small intestine may be obtained; thus, four of eight patients whose carcinoid was primary in the abdomen in our group of patients had been previously operated on elsewhere for this reason. Examination of tissue so removed will indicate the nature of the lesion.

Flushing.—A peculiar cutaneous flushing has been described by all who have written on this syndrome. It is perhaps the most outstanding physical finding when it is present, and remarkable descriptive terms have been applied to it.[2a]

fade from the center to the periphery, the central portion at first becoming dusky cyanotic before all color disappears and leaves this portion the color of normal white skin. At first glance these areas simulate giant hives, but they are not elevated above the surface of the skin.

There are reports that flushing can be precipitated by alcoholic beverages, hot drinks, eating, defecation, anger and anxiety, and by palpation of the enlarged liver or intra-abdominal tumor. However, investigators [21b] failed to demonstrate an increase of 5-hydroxytryptamine in the blood after ingestion of alcohol or food.

Diarrhea.—Diarrhea of varied severity occurred in 6 of the 12 patients. The number of stools ranged from a few to as many as 20 to 30 watery, yellow to green foul movements in 24 hours. When severe, diarrhea may occur at night as well as during the day; it is not bloody.

Asthma.—Three of the 12 patients gave histories of asthmatic attacks. The attacks were not severe and yielded readily to the usual medical measures. It has been suggested that the use of epinephrine be avoided in these patients.

TABLE 2.—*Features in Twelve Cases*

Feature	1	2	3	4	5
Flush	+	+	+	+	0
Diarrhea	0	0	+	+	0
Asthma	0	0	0	0	+
Heart murmur	0	0	0	Systolic pulmonic	0
Palpable liver	0	+	+	+	+
Abdominal mass	0	0	+	0	0
5-HIAA* in urine	+	+	+	+	Not examined
Serotonin in tumor, µg./Gm.	No data	Operation refused	Positive†	Operation refused	31
Carcinoid on biopsy	+	+	+	Operation refused	+
Proved metastasis	Mesenteric nodes, liver	Liver	Mesenteric nodes, liver	Operation refused	Liver
Primary lesion, site	Ileum	Ileum	Ileum	Probably small intestine	Left lower lobe of bronchus

* 5-HIAA = 5-hydroxy-3-indole acetic acid.
† Positive reaction obtained with 40 mg. of tumor tissue.
‡ Operation performed elsewhere.

Nine of our 12 patients presented historical and objective evidence of flushing at the time of examination and diagnosis. This symptom had been observed for periods ranging from a few months to 10 years. Flushes varied considerably in intensity, duration, and distribution. Some lasted only 30 to 60 seconds while others continued for several days; the majority lasted for only a few minutes. Two patients flushed almost constantly for a few months prior to death; the wife of one patient stated that he appeared very "red and healthy" as though he had a fresh sunburn and that he looked this way until he died.

Associated with the flush is an intense feeling of warmth, and at times rather severe perspiration occurs with the flush. Usually the head, neck, thorax, and arms are involved, though we have observed generalized flushing over the entire body. During a flush the skin appears florid. The scleras are injected. Red, blotchy, geographical areas with nonelevated edges may appear. These areas tend to

Pulmonic Systolic Murmur.—Three of our patients had a significant pulmonic systolic murmur, and two of these patients have died. Autopsy performed in one of these two patients did not disclose any significant change in the valves of the right side of the heart.

MacDonald [1b] reported that in 34 of the 57 cases of functioning carcinoid he reviewed there were proved, isolated, nonrheumatic lesions of the valves of the right side of the heart (or combined lesions on the right and left sides in the event of patent foramen ovale).

Liver Enlargement.—Enlargement of the liver with what was thought to be metastatic involvement at the time of physical examination was observed in 7 of the 12 patients. Involvement was proved surgically in 10 of the 12. One patient who refused exploration had a huge nodular liver that undoubtedly was involved in the metastatic process. In the only case in which the liver was proved surgically not to be involved and in which the post-

operative urinary levels of 5-hydroxy-3-indole acetic acid were normal, the carcinoid was in the gastrointestinal component of an ovarian teratoma.

Functioning Tumor Tissue Without Clinical Manifestations.—Functioning tumor tissue without clinical manifestations may be encountered, as in case 8. This case illustrates that large amounts of serotonin may be produced and that the urine may contain large amounts of 5-hydroxy-3-indole acetic acid in the absence of signs or symptoms of functioning carcinoid. Eventually this patient probably will have such signs and symptoms, but it seems at present that some bodily mechanism protects him from the abnormal amounts of serotonin being secreted. This case also indicates the value of postoperative determination of urinary 5-hydroxy-3-indole acetic acid in demonstrating the presence of metastatic functioning tumor tissue.

Site of Primary Lesion.—The site of the primary lesion was the small intestine in 7 of the 12 patients, the lesion being in the ileum in 5, in the jejunum in one, and in an unrecorded part in one. The primary lesion was in the cardia of the stomach in one patient, in the gastrointestinal component of an examined 1,120 specimens of urine from 1,023 patients and found that none gave the characteristic purple color, nor was any drug encountered which caused this color and thereby gave a false-positive reaction. He concluded that this qualitative test was highly specific for confirming the presence of metastatic carcinoid. If the results of the test are positive, the more informative quantitative determination [17] of the urine should be made. A 24-hour specimen of urine normally contains 2 to 9 mg. Higher values are abnormal.

It recently was reported [28] that ingestion of bananas led to increased excretion of 5-hydroxy-3-indole acetic acid in monkeys and in two children. Therefore one must be certain that bananas are not eaten during the period represented by the specimen of urine being collected.

In 10 of our 12 cases, qualitative tests gave positive results and quantitative tests yielded amounts of 5-hydroxy-3-indole acetic acid varying from 12 to 14 mg. to more than 280 mg. in 24 hours. In two cases this test was not done before operation. Further confirmation of the diagnosis can be obtained by analysis of the tumor for serotonin.

of Functioning Carcinoid Tumor

Case						
6	7	8	9	10	11	12
0	+	0	±	+	+	+
0	+	0	+	0	+	+
+	0	0	0	+	0	0
0	0	0	0	Systolic pulmonic	Systolic pulmonic	0
0	+	0	+	+	0	0
0	0	0	+	0	0	+
Not examined	+	+	+	+	+	+
86, 62	No data‡	345	No data	40	2,120	320
+	+	+	+	+	+	+
None (multiple adenomas of lung)	Liver	Liver	Mesenteric nodes, liver	Liver	None	Mesenteric nodes, liver
Lung, R. middle & lower lobes	Lung, R. lower lobe	Ileum	Ileum	Stomach	Teratoma, left ovary	Jejunum

ovarian teratoma in one, and, of most interest, in the lung in three, where apparently it was the carcinoid type of bronchial adenoma. The tumor tissue from the lung contained 31 mcg. per gram in one of the last three patients, and 86 and 62 mcg. per gram in another patient from whom two specimens were examined. The pulmonary lesion in the third patient was surgically removed elsewhere, and we did not have occasion to measure the tissue content of serotonin, though the tissue was reviewed and proved to be a bronchial adenoma of the carcinoid type on microscopic examination.

Laboratory Aspects

From the laboratory standpoint, confirmation of the clinical diagnosis of functioning carcinoid can be made by detecting abnormal amounts of 5-hydroxy-3-indole acetic acid in the urine. Reference was made to the simple qualitative test to demonstrate the presence of this substance. It was found subsequently that this is a reliable test. Mohler [27]

Three patients whose urine contained abnormal amounts of 5-hydroxy-3-indole acetic acid were given tryptophan after surgical proof of the presence of carcinoid. The tryptophan was administered in the morning, usually with breakfast. The effect of ingestion of this substance and also hydroxyzine and reserpine on the urinary content of 5-hydroxy-3-indole acetic acid is shown in table 1. The increase of the 5-hydroxy-3-indole acetic acid in the urine was small. This confirms previous observations by Udenfriend and suggests that tryptophan may be administered as a loading test, and if a functioning carcinoid is present, the majority of the administered tryptophan should be diverted over the serotonin pathway to the formation of serotonin and eventual degradation to 5-hydroxy-3-indole acetic acid, which will be present in somewhat increased amounts in the urine.

An additional confirming test has been proposed by Rotbart.[29] This test is based on the altered reactivity of the skin to serotonin. He injected sero-

tonin creatinine sulfate intradermally in the arms of two patients with functioning carcinoid. In the opposite arms of these patients he injected histamine phosphate and saline solution intradermally. He found that serotonin produced huge reactions with marked erythema on the flexor surface of the forearm and cyanotic fingertips in one patient. In the other there was marked erythema over a large area. In neither patient were the controls with histamine or saline solution comparable to the reactions induced by serotonin. Histamine wheals developed in 25 normal persons treated in a similar fashion, but the areas of erythema at the site of serotonin injections were no larger than the control areas. He proposed the thought that patients with malignant carcinoid syndrome hyperreact to intradermally administered serotonin as compared to the reaction of normal persons.

Management

The management of these patients presents many difficulties. It is felt that surgical removal of as much of the malignant tissue as possible is indicated. This should be done, especially where there are large metastatic masses involving mesenteric glands, in an effort to remove enough bulk of the tumor to reduce serotonin formation and thereby lessen symptoms. Caution in surgical intervention must be exhibited. Stacey [30] reported two instances in which an attack ultimately leading to death of the patient developed at an early stage in operation before any tumor tissue was manipulated. Similar difficulties have been encountered by Waugh.[31]

Much hope has been held that some of the reported antagonists of serotonin would be of value. As reported previously, our experiences with chlorpromazine have not been promising. According to others, brominated lysergic acid diethylamide has been tried, but Bean and Funk [26] did not note any change in signs or symptoms or diminution of excretion of 5-hydroxy-3-indole acetic acid after its use. They also reported a trial of 1-benzyl, 2-methyl, 5-methoxytryptamine hydrochloride in doses of 25 mg. three times a day for two weeks at a time without clinical effect or significant change in excretion of 5-hydroxy-3-indole acetic acid. We have used as much as 200 mg. of chlorpromazine a day and also hydroxyzine without any significant improvement.

Smith and co-workers [21b] stated that brominated lysergic acid had little clinical effect in their cases, although one patient appeared to excrete less 5-hydroxy-3-indole acetic acid. They also noted that reserpine provoked an over-all increase in flushing and frequency of bowel movements and that initially there was a marked increase in excretion of 5-hydroxy-3-indole acetic acid followed by a marked decrease, suggesting a period of relative depletion in the tissue. They proposed that this might be useful as a provocative test in nonsecreting cases.

Symptomatic measures may be helpful in attempts to control the diarrhea. The tranquilizing effect of chlorpromazine may have some value in this respect. Stacey [30] has stated that since excitement and norepinephrine may precipitate asthmatic attacks in these patients, the use of this drug in the treatment of bronchospasm may be inadvisable. If large amounts of histamine are being excreted in the urine, administration of one of the antihistaminics may be of value.

X-ray and radioisotope therapy have been tried in an effort to destroy metastatic tissue and reduce amounts of circulating serotonin. Two of our patients received extensive x-ray therapy with no obvious help. Stacey [30] reported on two patients who received x-ray therapy without benefit and with actual deterioration, though he stated that two additional patients received temporary amelioration after administration of radioactive gold.

Summary

The syndrome of functioning carcinoid is being recognized more frequently as knowledge of the clinical features and of confirmatory laboratory procedures is being more widely disseminated. The tumor functions in the same fashion as an endocrine tumor as a result of its secretion of serotonin.

Not all the clinical features need be present simultaneously to make the diagnosis. Demonstration of abnormal amounts of 5-hydroxy-3-indole acetic acid in the urine confirms the diagnosis. The amounts of this substance present in the urine may vary from time to time, and more than one determination may be necessary. Postoperative urinary determinations are of value in suggesting the development of metastasis.

The treatment of choice is surgical removal of all or of as much of the tumor tissue as is possible, to reduce the amount of serotonin secreted. Irradiation therapy is of doubtful value. To date, the "serotonin antagonists" have not been of aid in medical management. Symptomatic measures for relief of diarrhea, pain, and asthma are indicated.

The primary site of the lesion is usually the gastrointestinal tract, frequently the ileum. Three cases are presented in which the primary lesion in the patient was probably a bronchial adenoma of the carcinoid type.

Functioning carcinoids may exist with none of the clinical manifestations of the syndrome, as in case 8, in which large amounts of serotonin were present in tumor tissue and high urinary values for 5-hydroxy-3-indole acetic acid were found in the absence of any clinical evidence of the syndrome.

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NOTE: References 18 to 31, inclusive, will be provided by the authors on request.

EFFECT OF COMPETITIVE INDUSTRIAL ACTIVITY ON SEVERELY DISABLED CARDIAC PATIENTS

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Employers are reluctant to hire persons with cardiac disease even if they do not have a definite policy against it. Reasons for the reluctance in hiring these persons are reported to be that the physical demand of work exceeded the physical capacity of the cardiac patient; there is risk of monetary loss arising out of compensation claims; it is considered that cardiac patients are a heavy burden on company-sponsored insurance programs; there is insufficient medical staff; and it is not in accordance with the policy of the personnel department. Frequently, the detrimental effect of the psychological and emotional stress of a patient after ill-advised activity restriction is actually greater than that due to the cardiac involvement per se. The elimination of fear about heart disease is thought to be the major problem faced by the general practitioner in his efforts to rehabilitate patients with cardiovascular disease.

Much has been written in the recent medical literature regarding the employment and productivity of the cardiac patient, yet there has been no controlled study to evaluate the effect of competitive industrial activity on the diseased heart. Kline [1] gave a complete and detailed discussion on the method by which the problem of placement and evaluation had been successfully approached by the Work Classification Clinic of the Cleveland Heart Society. Hellerstein and Ford,[2] studying the oxygen consumption for workers in many listed so-called laboring jobs, found that this consumption is only two to three times the resting levels except for very short periods of time. Laplace [3] concluded that persons who have heart disease of slight to moderate severity are almost always capable of undertaking useful work.

Kline,[4] concerned with rehabilitation, stated that 45% of patients referred in the 2C to 3C classification (American Heart Association) were able to return to normal work activity. Black [5] said that the social and psychological conditions of the patient, his motivation and interest, are frequently much greater determinants for success in rehabilitation than the extent of his organic heart disease.

From the Human Resources Corporation, a division of Abilities, Inc.

Chapman,[6] of the U. S. Public Health Service, stated that most research has arrived at understanding the etiology of the heart disease and that added recent research studies explore the relationship between work and the development of heart disease, how best to measure the residual work capacity of the diseased heart, and how to relate the reserve capacity to the job demand.

Under a grant by the North America Insurance Company, a recent study was undertaken at Abilities, Inc., of Albertson, Long Island, N. Y., to evaluate the effect of work effort on the severely disabled cardiac patient. A detailed study was performed to evaluate the effect of competitive employment on the specific cardiac disabilities. This report first considers 10 patients with postmyocardial infarction with a history of one or more attacks and with varying degrees of myocardial decompensation. These persons would be considered unemployable in industry.[7] Also included in this study are the cases of seven persons with rheumatic heart disease and two with hypertensive heart disease.

Postmyocardial Infarction

Table 1 shows employee and employment data and degree of change that has taken place in the specific disability of 10 patients since being employed. In these patients, all with heart disability due to coronary artery disease with myocardial infarction, the age spread was from 26 to 63 years. One patient was 26 years of age, one was 48, and the rest were over 50. Each patient revealed some degree of decompensation at rest while receiving medical therapy. All have or have had electrocardiographic evidence of myocardial infarction. The elapsed time from the first incident of infarction to the time of writing ranged from 1 to 10 years. Three persons had a history of proved secondary attack. There is a wide range in the type of work per-

TABLE 1.—*Employment and Illness Data for Ten Men with Myocardial Infarction Employed at Abilities, Inc.*

			Work		Travel			Employment Data*			Illness Data	
Case	Age, Yr.	Disease	Type	Effort Required	Time, Min.	Distance, Miles	Mode	Time Employed	Period of Evaluation, Yr.	Absence due to Specific Illness, Days	Degree of Change	Anginal Attacks
1	62	Myocardial infarction (1951); hypertension; angina pectoris after exertion; class 2C	Office	Active	45	19	Drives	9/56—present	1 5/12	None	Compensated; no change	Minimal attacks since employment; no glyceryl trinitrate taken in 3 months
2	52	Myocardial infarction (1957); angina pectoris; congestive heart failure; class 3C	Bench work, coil winding	Sitting job	40	20	Drives	11/56—3/3/58	1 1/6 ...	...	Change from class 2B when employed to 2A	Need for glyceryl trinitrate dropped from 15+ tablets per day to 1-5; stroke occurred 2/25/58 at home; died 3/3/58
3	62	Myocardial infarction (1951); disabled 4½ yr.; class 3C	Bench work, electrical	Sitting job	20	10	Car pool	4/56—3/58	1 5/6	14	Walking endurance increased from ½ to 4 blocks; little dyspnea	None
4	59	Myocardial infarction (1958); angina pectoris with and without effort; second attack, 1954; digitalis and glyceryl trinitrate therapy; class 3C	Electronics	Sitting job, moderate activity	35	11	Drives	5/57—present	1 3/4	None	Definite improvement; change from class 3B when employed to 2B	Need for glyceryl trinitrate dropped from 10+ tablets daily to only 6 in 3 months
5	26	Myocardial infarction (1954); familial hypercholesteremia; angina pectoris on effort; second attack, 1955; class 2B	Office	Walking, etc.	20	5	Drives	9/56—present	1 5/12	13½	Compensated; pentaerythritol and heparin prescribed	4-5 attacks daily increased to 5-10 since employment
6	63	Coronary artery disease; infarction (1949); left hemiplegia, 1952; compensated; premature ventricular contractions	Coil winder	Sitting and some standing	15	7	Drives	3/56—3/58	1 3/4	None	Compensated; left hemiplegia; no change	None
7	56	Myocardial infarction (1953); compensated	Mechanical	Sitting job	30	12	Drives	2/56—present	2	6	Compensated; no change	None
8	48	Myocardial infarction (1955); second attack, 1955; compensated	Office, purchasing	Active	30	12	Drives	4/56—present	1 5/6	None	Compensated; no change	None
9	60	Myocardial infarction (1956); angina pectoris on effort; hypertrophied heart; compensated	Electrical	Sitting job, active	30	7	Car pool	4/56—present	1 5/6	None	Compensated; less premature ventricular contractions	Attacks rare when working; walking endurance from ¼ to 6 blocks
10	62	Myocardial infarction (1952); auricular fibrillation; enlarged heart; irregular rhythm; class 3B	Bench work, mechanical	Sitting job	45 "	12	Car pool	8/53—present	4 1/2	None	Class 2B when employed; no change	None

* All were examined in September, 1957; none had compensable accident rate.

formed by these employees. It will be seen from table 1 that many of the employees were physically active as far as walking is concerned, but none of them were employed in any occupation that requires heavy labor. The travel time, distance traveled, and mode of travel have been recorded. The strain of driving or riding (by means of a car pool) through heavy city traffic may be a factor in the final evaluation of the progress made by these employees. The time traveled ranged from a minimum of 15 to a maximum of 45 minutes each day. The distance traveled ranged from a miniumum of 5 to a maximum of 30 miles. Seven of these employees drove their own cars, whereas only three were driven to work by means of a car pool.

All of these employees had been at Abilities, Inc., for more than one year except for one (case 4), who was employed in May, 1957. The absenteeism due to the specific illness may be noted to be somewhat remarkable. There was one death (case 2); the patient sustained a cerebral embolism on Feb. 27, 1958, while at home, and died March 3, 1958. This employee had, in the previous week, been trapped in a snowstorm in his car and exerted himself to a rather high degree for over one and one-half hours. This had precipitated a mild left ventricular failure which required several days' rest at home. Although he returned to work after the episode, for some reason he did not fully recover. In the list of compensable accident rate, it will be noted that not one of these employees sustained an accident while employed at Abilities, Inc.

Four patients have shown no evidence of any change in cardiac status since employment. One patient (case 9), who had an enlarged heart with multiple premature ventricular contractions, which condition was compensated, on reexamination revealed less premature ventricular contractions, to the degree that they were now only rarely found. The patient in case 2, who had congestive heart failure and improved so remarkably, was the man who died March 3, 1958, from cerebral embolism. The 62-year-old patient in case 3 had rather severe coronary artery disease with myocardial infarction and evidenced an advanced decompensation manifested by edema, dyspnea on effort, digitalis bradycardia, and fluid in his chest. He required meralluride (Mercuhydrin) sodium injections three times weekly and, at the time of writing, finds that his walking endurance has increased from one-half to four blocks with very little dyspnea.

Table 1 reveals that 5 of the 10 listed patients with postmyocardial infarction who were employed at Abilities, Inc., showed no change since being employed, 3 showed definite improvement, 1 died, and 1 (case 5) seemed to have an increase in anginal attacks but no increase in disability. The column on anginal attacks is remarkable in several respects. It will be noted that four out of five persons who had anginal attacks were very definitely improved in spite of an increase in their physical activity. The 62-year-old man in case 1, who showed no change in his myocardial status and who had a history of multiple angina attacks on effort (mild effort produced attacks requiring glyceryl trinitrate [nitroglycerin] therapy), found that since the time of employment these attacks have been minimal. He has not had to take any glyceryl trinitrate tablets at all during the three months prior to time of writing. A similar history was obtained from the employee in case 4; frequent anginal attacks which required 10 to 15 glyceryl trinitrate tablets daily have, since the time of the patient's employment, been reduced markedly. This patient has taken only six tablets of glyceryl trinitrate during the three months prior to time of writing.

CASE 2.—A 52-year-old man was employed at Abilities, Inc., in November, 1956, in a sitting job. His medical history showed that he sustained a myocardial infarction in 1951, accompanied by congestive heart failure. He had angina pectoris on effort, requiring 15 to 30 tablets of glyceryl trinitrate daily. He was on a salt-free diet but exhibited symptoms of congestive heart failure, that is, shortness of breath after exertion, orthopnea, and edema of both lower extremities.

Since employment, he had been on therapy with a rigid salt-free diet and one tablet of pentaerythritol tetranitrate-alseroxylon (Pentoxylon) three times a day. He drove back and forth to work each day. This man had been unemployed for 16 months prior to being hired by Abilities, Inc., because of his chronic congestive heart failure. At the time of the examination, he had noticed a marked improvement in his ability to walk several blocks without undue breathlessness. Roentgenograms of the heart and chest showed a myocardial enlargement of moderate degree, with some perihilar congestion but no free fluid.

He had suffered one mild attack of left ventricular failure. This followed prolonged exposure during a snowstorm when he could not start his car. He was put on chlorothiazide (Diuril) therapy, 500 mg. three times a day, and responded so well that he was back to work in four days. An electrocardiogram taken on Feb. 24, 1958, did not reveal any new infarction, but on Feb. 27, 1958, he developed a left-sided hemiplegia while at home. He died on March 3, 1958.

The only change in the medical regimen of this employee since he was hired was the addition of pentaerythritol–alseroxylon and the advice of more rigid control of his salt intake. The effect of employment had certainly not been detrimental, and his condition was satisfactory until he exerted himself violently during the snowstorm previously mentioned.

CASE 3.—A 62-year-old man developed a myocardial infarction in 1951, at which time he was hospitalized for 31 days. He had a grade 4 decompensation and was kept at home until April, 1956. During his home care, he was constantly digitalized and received mercurial injections three times a week. He exhibited orthopnea, cyanosis of the skin, and a short, disturbing cough. He developed diabetes mellitus in 1953. Electrocardiograms revealed extensive heart damage, left ventricular hypertrophy, evidence of old myocardial infarction, digitalis bradycardia, first degree heart block, and intraventricular conduction delay.

He was employed at Abilities, Inc., on April 16, 1956, without receiving a preemployment physical examination. He was examined on Jan. 29, 1957, at which time he revealed moderate dyspnea on effort, no cyanosis, moderate pallor, blood pressure of 140/100 mm. Hg, and no neck vein

pulsations. The heart was enlarged to the left in the sixth interspace to the mid-axillary line. No thrills were palpable. The sounds were regular, with only occasional premature contractions. The rate was 80 beats per minute. There was a grade 2 apical systolic murmur, with no radiation. Examination of the lungs revealed dulness at the right base, with diminished breath sounds; no rales were audible. The abdomen was obese; the liver was enlarged four fingerbreadths, there was no fluid wave nor shifting dulness, and no hernia was found. There was edema (3+) of both lower extremities from the foot to the knee.

The patient was reexamined in November, 1957. Therapy with digoxin, 0.25 mg. was reduced from one dose per day to one every other day, while that with acetazolamide (Diamox) was reduced to 250 mg. taken in the morning every other day. His mercurial injections were reduced from three weekly to one a week. There was no change in the heart size, but the premature heart beats were now rarely heard. The liver was no longer enlarged, and the edema was now confined to the ankles only and was rated as 1+. His diabetic status since the time of employment has been controlled by diet. Breathlessness on effort, however, was still present at the time of writing.

The patient has shown dramatic improvement since being employed. Although formerly considered a completely decompensated individual who had been forced to remain at home for four and one-half years after his myocardial infarction, he has shown remarkable clinical improvement during the time he has been gainfully employed.

Case 4.—A 59-year-old man was employed in May, 1957, at a job where he sits all day and does light manual labor. His history revealed that he sustained a myocardial infarction in 1948 and a secondary attack in 1954. He had been completely disabled for two years prior to being employed at Abilities, Inc. He had multiple attacks of angina pectoris with and without effort. These attacks were relieved by sublingual administration of glyceryl trinitrate, and he takes 0.2 mg. of digitoxin daily at present.

He was examined on Sept. 9, 1957, four months after beginning his present work. At that time, he revealed shortness of breath on effort but no edema and no nocturnal dyspnea. He used only 6 glyceryl trinitrate tablets in the following six months, whereas previously he used 5 to 10 tablets daily. Examination revealed a well-nourished, gray-haired man. There was a moderate degree of arcus senilis and no neck vein pulsation. The heart was enlarged to the left anterior axillary line in the sixth interspace, and no thrills were palpable. The first heart sound at the apex was soft, while the second sound was accentuated and snappy. There was a harsh, shrill, grade 4 apical systolic murmur, with radiation to the left axilla, and regular sinus rhythm at the rate of 82 beats per minute. The lung fields were clear; the liver was not enlarged; and the blood pressure was 184/130 mm. Hg.

This man showed little change in his physical status after a period of employment. However, there was a definite improvement in his sense of well-being and a decrease in number of anginal attacks.

Table 2.—*Employment and Illness Data for Seven Persons with Rheumatic Heart Disease Employed at Abilities, Inc.*

			Work		Travel			Employment Data‡			Illness Data	
Case*	Age, Yr.	Disease†	Type	Effort Required	Time, Min.	Distance, Miles	Mode	Time Employed	Period of Evaluation, Yr.	Absence due to Specific Illness, Days	Disease Stability and Compensation†	Specific Effect of Work
11	37	Rheumatic heart disease; auricular fibrillation; hypertrophied heart; mitral insufficiency; mitral stenosis; class 3C	Inspector	Walks, sits	30	11	Drives	4/57—present	5/6	14 ½	Taking digitalis, mercurials; regulated diet	Condition generally improved; needs less mercurials, but still requires digitalis, salt-free diet; dependent edema almost negligible
12	24	Rheumatic heart disease; hypertrophied heart; mitral insufficiency; mitral stenosis; auricular fibrillation; aortic insufficiency; class 3B	Office work, messenger	Walks, sits	40	15	Drives	9/57—present	5/12	6	Laryngoparalysis, recurring nerve on one side causing hoarseness; pulmonary infarction, 1955. Prescribed less salt in diet, digitalis, prophylactic penicillin therapy	No change
13	56	Rheumatic heart disease; aortic stenosis; mitral insufficiency; mitral stenosis; valvulotomy, 2/14/56; RSR; class 3A	Bench work, electrical	Sits	25	15	Drives	9/57—3/58	5/12	3 (2-mo. leave of absence)	No change	Condition improved since employment; only medication is penicillin prophylactically
14	22	Rheumatic heart disease; aortic stenosis; mitral insufficiency; mitral stenosis; enlarged heart; RSR; class 3B	Mechanical	Walks, sits	20	6	Car pool	6/56—2/58	1 ⅝	None	Prescribed digitalis, 0.1 mg. daily, less salt in diet, prophylactic penicillin therapy; RSR	No change
15	55	Rheumatic heart disease; auricular fibrillation; mitral insufficiency; enlarged heart; class 3B; diabetes mellitus requiring insulin	Bench work, harness and cable department	Sits	30	7	Car pool	5/56—present	1 ⅝	2	Takes digitalis and insulin	No change
16	43	Rheumatic heart disease; hypertrophied heart; auricular fibrillation; mitral insufficiency; class 3B	Bench work, electrical	Sits	20	8½	Drives	4/57—present	5/6	2	Takes digitalis daily	No change
17	43	Rheumatic heart disease; aortic stenosis; RSR; class 2B	Packaging	Heavy activity, lifting, operates machinery	30	10	Drives	2/56—present	2	None	Change to class 1B	No change

*All were men except patient in case 15.
†RSR=Regular sinus rhythm.
‡All were examined in September, 1957; none had compensable accident rate.

Rheumatic Heart Disease

Table 2 lists seven employees with rheumatic heart disease with some degree of valvular deformity. Four had a disturbance of rhythm classified as auricular fibrillation, one had a complication of diabetes mellitus and required insulin therapy, and one had a finger fracture valvulotomy on Feb. 14, 1956. The type of work is indicated, and it can be seen that this work entails physical activity of a competitive nature of varying degrees. The time involved in traveling to work ranged from 20 to 40 minutes and the distance traveled from 6 to 15 miles each way. The column on mode of travel to and from the plant shows that five of these employees drive their own cars while only two make use of a car pool.

It is also seen that in these patients the remarkable compensable rate of zero in each case is similar to that found in table 1 relating to persons with cardiac disease due to myocardial infarction. In regard to absenteeism as a result of the specific illness, only one person was absent due to a temporary decompensation. This employee was absent for 14 days and four hours and, back at work, showed a return to his previous status. The remaining six employees had no absences due to their cardiac disease.

Also listed in table 2 are the disease stability and compensation of the rheumatic group. Six of these patients are still under constant medical observation and are treated with cardiotonic drugs, as well as a low-salt diet and mercurials, to maintain their compensation. Only one patient (case 17), with aortic stenosis, does not at the time of writing require any form of medication. On the specific effect of work since employment began, two patients showed definite improvement, in that they now require less mercurials and have been able to increase their physical activity. The other five have shown no change in cardiac status.

Case 11.—A 37-year-old man had a history of rheumatic fever beginning at the age of 12. He was apparently normal until the age of 30, when he developed shortness of breath on effort, with chest pains. He has had frequent colds since childhood and had become incapacitated and unemployable at the age of 33.

Previous to his employment at Abilities, Inc., a report from Meadowbrook Hospital stated that he was hospitalized on Dec. 1, 1956, and discharged Dec. 21, 1956. His diagnosis at that time was given as pulmonary infarction and rheumatic heart disease, with enlarged heart, auricular fibrillation with bradycardia, murmur of mitral stenosis, mitral insufficiency, and Graham Steell congestive heart failure, class 4E.

The chest x-ray taken Dec. 1, 1956, revealed a heart markedly enlarged in all chambers and pulmonary consolidation in the right mid-lung field laterally. There was an increase in the left pulmonary artery pattern. His lung bases were clear, and there was no evidence of pleural fluid. Another roentgenogram taken Dec. 4, 1956, did not reveal any changes except that the possibility of pericardial effusion was considered. A third roentgenogram taken on Dec. 7, 1956, showed massive cardiac enlargement to both the right and the left. All chambers were still enlarged. There was a tremendous enlargement of the left atrium, with elevation of both main stem bronchi and marked posterior displacement of the barium-filled esophagus. A patch of density in the mid-portion of the right lung field was seen, which appeared to be parenchymal infiltration and may have represented an area of pneumonitis. No pleural fluid was noted. A fourth roentgenogram taken Dec. 12, 1956, showed no change except for some blunting of the right costophrenic sulcus.

The report on an electrocardiogram taken Dec. 1, 1956, was as follows: auricular fibrillation, prolonged intraventricular conduction, and right ventricular preponderance with possible hypertrophy. Electrocardiograms done on Dec. 10 and Dec. 20, 1956, showed no change from the previous tracing.

The patient's therapy during that hospitalization included rest, intramuscular injections of 2 cc. of meralluride daily, 0.25 mg. of digoxin given twice daily, and 500,000 units of penicillin given orally daily.

This man was hired in spite of his rather advanced rheumatic heart disease and was placed on a job of inspection, which required several hours of slow walking daily. He was examined in October, 1957, after working for six months. The cardiac findings were as follows: The heart was enlarged to the sixth interspace and to the left anterior axillary line. A moderate diastolic thrill was felt in the fifth interspace at the midclavicular line. A slight precordial heave during systole was noted in the third left interspace. On auscultation, a slapping first sound was present at the apex, while the second sound was soft and barely audible. A grade 1, blowing, soft, apical systolic murmur and a grade 3 harsh diastolic murmur with radiation to the left axilla was heard. The pulmonic second sound was accentuated and louder than the aortic second sound. Auricular fibrillation at the rate of 68 beats per minute was present. No Graham Steell murmur was audible.

Examination of the lungs showed the chest to be barrel-shaped, with hyperresonance on percussion over both lung fields outside of the cardiac area. Breath sounds were distant and equal, but persistent inspiratory and expiratory sibilance over both upper lobes was heard. The liver and spleen were not palpable; no dependent edema was present. Chest x-ray revealed marked cardiac enlargement in all directions, with some perihilar congestion. The diaphragms were flattened, and the costophrenic angles were clear. The electrocardiogram showed right ventricular hypertrophy, auricular fibrillation, and digitalis effect. The erythrocyte sedimentation rate was normal, and the complete blood cell and differential counts were normal. The employee is at present on therapy with digoxin, 0.25 mg. daily, meralluride, 2 cc. given intramuscularly once weekly, chlorothiazide, 500 mg. daily, and prophylactic doses of penicillin, 200,000 units daily given orally.

On Feb. 13, 1958, this employee caught a cold with a severe cough which responded well to chlortetracycline (Aureomycin) hydrochloride, 250 mg. given four times daily. He was out of work for two days. No change in his cardiac status occurred.

The employee has performed well while at work. He drives himself to and from work by automobile through city traffic. Absenteeism due to his cardiac status has not occurred. The employee states that since his employment he can walk greater distances than previously and suffers less breathlessness on effort.

Case 12.—A 24-year-old man was employed in September, 1957, and given a job as office boy, requiring walking and sitting. His history of rheumatic fever began in 1940; a second attack occurred in 1947, and at that time a heart condition was found. In 1955, he developed a cough and fever, hemoptysis, and auricular fibrillation. He was hospitalized at Montefiore and King's County hospitals in New

York and Brooklyn, N. Y. He developed a persistent hoarseness in 1955. His present medical regimen consists of prophylactic penicillin therapy; digitalis; theophylline, ephedrine, hydrochloride, and phenobarbital tablets (Tedrol); phenobarbitol; and a low-salt diet. At the present time, he does not complain of any breathlessness or cough.

Examination revealed a tall, thin young man with no cyanosis and no dyspnea. He had marked hoarseness, no neck vein pulsation, and no filling of neck veins on liver pressure. His blood pressure was 134/0 mm. Hg. The heart was percussed to the left mid-axillary line in the sixth interspace and to the right parasternal line. There was a suggestive systolic thrill in upper midsternum area and a slight heave at the left third interspace on systole. The heart sounds were completely irregular. The pulmonic second sound was accentuated, and there was a grade 3 apical systolic blowing murmur and a grade 2 diastolic murmur heard best over Erb's point with radiation to the neck. The first aortic sound was inaudible. The lungs were resonant to percussion. The breath sounds were altered by some harshness of the expiratory note over the lung bases and some sibilance. The liver and spleen were not palpable.

The diagnosis was rheumatic heart disease, auricular fibrillation, mitral insufficiency, mitral stenosis, and aortic insufficiency with decompensation. The patient was classed 3B. The left recurrent laryngeal nerve was paralyzed due to pressure from the enlarged heart.

Laboratory findings on Feb. 10, 1958, were as follows: red blood cells, 4,100,000 per cubic millimeter; white blood cells, 7,300 per cubic millimeter, with polymorphonuclear cells, 71%, and lymphocytes, 29%; and hemoglobin level, 12.5 Gm. per 100 cc. Urinalysis revealed the specific gravity to be 1.008; tests for albumin, sugar, and acetone were negative; and the urine was normal on microscopic examination.

The electrocardiogram showed right ventricular hypertrophy and auricular fibrillation, and x-ray of the heart revealed all heart chambers to be enlarged (cor bovinum). At reexamination on Feb. 26, 1958, there was no change in these findings.

Although this employee had a badly damaged heart, he has maintained compensation after several months of productive active work, including traveling to and from his job. He has been absent four days, without compensation.

CASE 15.—A 55-year-old woman was employed on May 14, 1956, and given a sitting job at a bench. She previously had been employed as a switchboard operator. She gave a history of "rheumatism," beginning at the age of 29, and was told that she had heart trouble at the age of 54. This history was inadequate because the employee denied any cardiac examination for many years. At the time of writing, she had been on digitalis therapy for 10 months. Since being employed at Abilities, Inc., she has been fairly well and no longer complains of breathlessness on effort. Ankle edema, present when she was hired, is no longer evident. She developed diabetes mellitus in 1956; this has been controlled by diet and injections of protamine zinc insulin 12 units daily.

Examination showed no dyspnea and no cyanosis. Her blood pressure was 120/80 mm. Hg. Heart percussion showed enlargement to the left 2 sonometers outside the midclavicular line in the fifth interspace. No thrills were palpable. Heart sounds were distant. There was an apical, grade 1 systolic murmur and no radiation. The lungs were clear to percussion and auscultation. Examination of the abdomen revealed no masses; the liver and spleen were not palpable; and there was no dependent edema.

The patient was given a classification of rheumatic heart disease with mitral insufficiency, auricular fibrillation, and digitalization and was categorized in class 2B.

An electrocardiogram taken on Feb. 26, 1958, revealed right ventricular hypertrophy with vertical heart, digitalis effect, and auricular fibrillation. A chest roentgenogram taken on Jan. 16, 1958, showed that the thoracic cage was normal and lung fields clear. The left cardiac border was straightened, but the heart did not appear enlarged. A complete blood cell count done Feb. 7, 1958, gave the following findings: red blood cells, 5,060,000 per cubic millimeter; white blood cells, 8,900 per cubic millimeter, with polymorphonuclear cells, 56%, and lymphocytes, 44%; and hemoglobin level, 14 Gm. per 100 cc. Urinalysis on that date showed the specific gravity to be 1.022; tests for albumin and acetone were negative; the glucose findings was 2.4% (3+); and results of the microscopic examination were normal.

Hypertensive Heart Disease

In this study, there were only two employees with hypertensive heart disease. One, a 62-year-old woman, had auricular fibrillation. In addition, a nodule, about the size of a small pea, was present in the left upper lobe of the thyroid gland. The other employee, a 54-year-old woman, had angina on effort and required 30 tablets of glyceryl trinitrate a day. She also had complicating diabetes mellitus which required 40 units of protamine zinc insulin given daily. In neither case was there overt evidence of congestive failure. Their type of work does not require too great a physical effort. One does coil winding, a sitting job, and the other clerical work, also a sitting job. The travel time is 45 minutes for one and 60 for the other each way, and the distance traveled is 11 and 13 miles respectively. Both of these patients traveled to and from work by means of a car pool.

The starting date of employment at Abilities, Inc., was November, 1956, for the first and August, 1957, for the second. Absenteeism due to the specific illness has been zero for both. No accidents have occurred during the time employed, which is up to the time of writing for both employees.

The first patient has had no change in cardiac or hypertensive status. The second, who had angina pectoris on effort for five years previous to employment and required 30 glyceryl trinitrate tablets daily, now takes only 3 per day. This change in status of angina pectoris has taken place gradually over the past three years. There has been no change in hypertensive or diabetic state.

Comment

A report by Olshansky and associates,[7] on cardiac patients in the greater Boston area, revealed that employers are reluctant to hire such persons even if they do not have a definite policy against it. Only 99 persons known to have cardiac disease were hired among 13,431 workers during a six-month period. Kline[4] reported that the physical demand of work exceeded the physical capacity of the cardiac patient and was listed by 71% of the industrial physicians surveyed as a major reason for reluctance in hiring these persons. Next in order of importance was the risk of monetary loss arising out of compensation claims (42%); consideration that cardiac patients are a heavy burden on company-sponsored

insurance programs (30%); insufficient medical staff (12%); and policy of personnel department (11%). Only 8% of the physicians surveyed considered cardiac patients to be unsafe workers, and only 3% considered them to be inefficient. Lee and associates [8] also found that the threat of monetary loss from compensation claims, sickness benefits, or pension benefits is a major reason cited by industry for reluctance to hire persons with cardiac disease. They found that 9 out of 19 industries had a stated policy to hire such persons, 7 had a definite policy against hiring them, and in 3 this information was not available. Eight industries revealed that cardiac patients had been hired during the past year, and, in this period, 242 persons known to have cardiac vascular disease were among the total of 19,321 new workers employed. Asymptomatic hypertension was the most common diagnosis, followed in order by rheumatic heart disease, heart disease, type undetermined, and arteriosclerotic heart disease. Actually, only 24 new employees had been given a diagnosis of arteriosclerotic heart disease, despite the frequency of this disease in the adult male population of the United States. All 19 industries reported, however, that it was their policy to return an employee to his job after recovery from an acute heart attack. The need for more facts regarding the work experience of cardiac patients was stressed.

Jezer [9] states that "the work experience of rheumatic cardiacs who show auricular fibrillation is very poor, and their rate of absenteeism is much higher [than cardiacs with minor arrythmias], because the arrythmia is usually associated with advanced heart disease, congestive heart failure, and, frequently, peripheral embolization."

The literature is replete with reports showing "cardiacs" to be safe workers,[10] especially when properly placed; usually they have a higher average productivity than persons without cardiac disease, and the turnover among this group is below the average for the latter group.

Frequently, the detrimental effect of the psychological and emotional stress of a patient after ill-advised activity restriction is actually greater than that due to the cardiac involvement per se.[11] Another report [12] stated that occupational activity does not necessarily lead to progression of heart disease or deterioration of the physical condition of the patient. As a matter of fact, a substantial number of patients with cardiac disease show improvement while in an employed status. This conclusion was based on a study of 580 patients with various cardiac diseases. Lee and co-workers,[8] in a questionnaire survey of general practitioners, concluded that the experience was favorable in patients returning to work after an acute myocardial infarction. Most of the patients were able to return not only to work but to their previous occupations without a great deal of restriction. It was thought that advice from the physician regarding the ability of the patient to return to work and to a useful, productive life should be included in his discussion with the patient. The elimination of fear about heart disease was thought to be the major problem faced by the general practitioner in his efforts to rehabilitate patients with cardiovascular disease.

Conclusions

This report on 19 employees, all classified as having severe or advanced heart disease, may be considered unique in that never in the history of private industry has such a deliberate policy of employing the "unemployable" cardiac patients been seen. The financial success of this enterprise is evidence of the productivity of these employees. The maintenance of excellent attendance records, and not one reported case of compensable injury, is directly contrary to the stated reasons given by industry for not employing cardiac patients. The absence of any detrimental effect of employment on the disease state is well documented in the literature, and the remarkable improvement exhibited by some of the employees makes one wonder whether the dictum that the person with severe cardiac disease requires constant rest and should retire from employment should not be revised to this: Employment in a compatible job can, in the specific case, be beneficial.

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LOWER EXTREMITY SKIN COVERAGE IN CHILDREN

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Short cuts for supplying adequate skin coverage to the lower extremity in children, especially those below the age of 10, are mandatory. It is not practical to place a child in a cross-leg flap position or to attempt distant pedicle procedures. Comparison between the adult and the child can be made in practically every circumstance, from the problem of the simple small superficial coverage to that of the larger deep areas.

In an extensive burn in an adult, when the postage stamp skin graft method is used, there is good healing of the grafts; however, the grafts are placed closer together in the adult in order to get quicker epithelization between them. The scarring between the postage stamp grafts is more evident in the adult. It may take months before the dark blue color between the postage stamp grafts will disappear, because of poor circulation. It is also necessary to support circulation of the entire lower extremity with elastic bandages for many months. In the child, a more complete coalescence of postage stamps with sturdier epithelium takes place, and new superficial venous channels spring up in a relatively short time. Little of the multiple-square appearance that shows up in the adult postage stamp grafting is evident in the child.

In the adult, tendon exposure for any length of time means almost certain death to the tendon unless a flap or tube pedicle can be applied for coverage. This requires many stages and extensive casting, which is almost impossible in children below the age of 10. In a child, when tendon exposure occurs there will often develop a granulation tissue covering from the surrounding areas within 10 to 14 days. This is less time than it would take to prepare an abdominal-pedicle or a cross-leg flap. This granulation bed will take an adequate skin graft, which after several months develops an areolar layer of tissue and a satisfactory pliable coverage.

This was the situation in a child who had suffered a severe crush injury (fig. 1). Split thickness skin grafts were used to cover the granulation tissue as soon as the tendons were covered. Multiple drill holes were placed in the small area of exposed bone at the time of split grafting. The grafts took completely. Within two weeks granulation tissue grew out of the drilled bone, and this smaller area healed spontaneously.

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In the child with an extensive burn, a more complete coalescence of postage stamp grafts, with sturdier epithelium, takes place, and new superficial venous channels spring up in a relatively short time. When tendon exposure occurs there will often develop a granulation tissue covering from the surrounding areas within 10 to 14 days. This is less time than it would take to prepare an abdominal-pedicle or a cross-leg flap. Long-standing immobilization of a joint of a child or exposure of the joint of a child are not the major problems that they are in the adult. Comparison between the adult and the child, from the problem of the simple small superficial coverage to that of the larger deep areas, can be made in practically every circumstance.

In the adult, exposure of the Achilles tendon, with loss of surface coverage, requires a full-thickness skin flap with subcutaneous tissue. The cross-leg type flap is used to get satisfactory coverage and function. In children, exposure of the Achilles tendon is not as alarming a problem (fig. 2). These wounds first require a good surgical débridement. This is sometimes followed by the use of enzymatic débridement agents to hasten cleaning of the wound. It may take several days with daily applications to help débride remaining areas that could not be cleaned surgically. A single thickness of fine mesh gauze, which need be changed only once a day, should be used over the wound. (This is used to prevent pain when the dressing is changed and also to help keep granulations flat.) Above this, warm saline dressings should be applied every three hours during the day and every four hours during the night. When a good clean granulation coverage has been obtained, a split skin graft is then used. A pliable areolar layer develops under the split-thickness skin graft, and the Achilles tendon then functions satisfactorily. No further coverage is ordinarily necessary. If lengthening of the Achilles tendon is necessary at a later age due to hindered growth, then a cross-leg flap can be done at the more opportune age.

In the adult, tibial exposure with chronic ulceration almost always requires an abdominal-tube pedicle or cross-leg flap coverage in the event a

bone graft is necessary. In children, tibial exposure is usually not serious. Most bone exposures will cover with granulation tissue. The use of multiple drill holes in the cancellous bone is reserved to promote granulations for earlier grafting in wider areas of exposure. Usually this coverage can be obtained within a two-or-three-week period by split skin grafts. There has never been a case of post-traumatic nonunion in the tibia of a normal baby or young child in the Milwaukee Children's Hospital.

In the adult, exposure of the calcaneus by a cast pressure sore may be as major a problem as the original injury for which the leg was placed in a cast. The area may require the placement of a cross-leg flap for adequate coverage. In children the calcaneus exposures do occur from time to time in legs which have been in casts for long periods of time (especially those which may have had femur fractures with traction). Here again, multiple holes can be drilled into the bone. After adequate necrotic tissue débridement and wet dressings, a clean granulation tissue covering will form in two to three weeks. A split graft at this stage will adequately handle the problem.

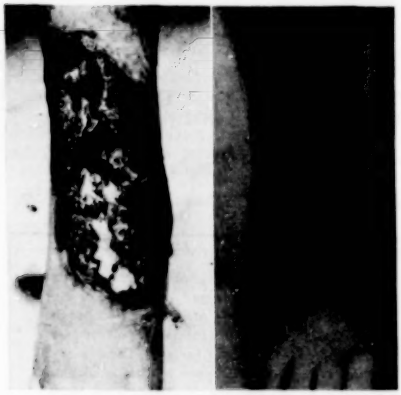

Fig. 1.—*Left*, débridement after crush injury of dorsum of foot. Demonstrates mechanism of granulations over tendons to give protective coverage in child. *Right*, adequate skin cover, in same child, provided by split skin grafting directly over granulations covering tendons. Areolar layer develops in six or more months for adequate gliding.

In the adult, joint exposures usually mean permanent stiffness with extreme inadequacy of the joint. It may even be serious enough so that arthrodesis or arthroplasty may be required later. In children an open joint will seal and heal almost miraculously, many times without apparent damage to its mobility.

In a severe acute injury with tissue loss and bone, tendon, and nerve exposure in the adult, the surgeon must be cautious in using local primary rotation flaps for coverage of vital structures below the knee. The chances of poor flap circulation without the use of delay procedures are increased lower on the leg. Consequently, all one can do initially is to resort to split skin grafts for avulsed areas and the utilization of the safer double-pedicle flap as much as possible. The more extensive rotation flaps may be used as possible secondary procedures in the adult.

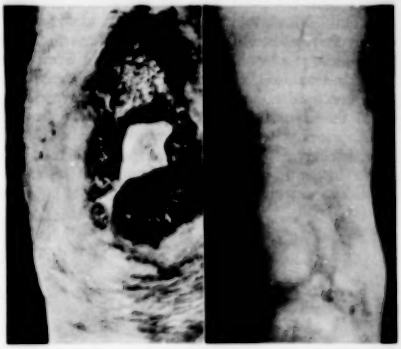

Fig. 2.—*Left*, granulation tissue, in child, creeping over exposed Achilles tendon and portion of calcaneus. *Right*, split skin graft coverage, in same child, adequate over granulations which had completely covered Achilles tendon and calcaneus. Areolar tissue developed under split skin graft for adequate skin mobility above tendon.

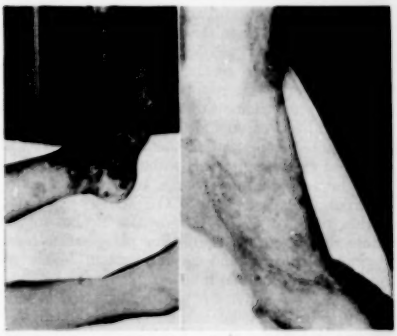

Fig. 3.—*Left*, avulsion of skin dorsum of foot of child with exposure of tendons, nerve, and bone. Considerable amount of dirt and black grease in wound. *Right*, foot of same child after healing effected by thorough wound cleansing and primary rotation flaps to cover tendon, nerve, and bone, with adjacent split skin grafting.

In the avulsion injury in the child, much can be done with the initial use of primary rotation flaps, even on the foot, with relative safety. When there is exposure of bone and tendons, if the patients are received early, many hours of time and repetitious surgery can be saved. This is illustrated in the case of a child whose foot was run over by a car and in whom there was avulsion of the skin exposing tendon, nerve, and bone (fig. 3). Rotation flaps were immediately used, after thorough wound cleansing, to cover tendon and bone. Split skin was used to cover the areas from which these flaps were taken. Thus, primary healing was effected with good function, saving many additional weeks of hospitalization. This same procedure could not have been successfully consummated in the adult.

Conclusions

A primary well-healed wound of the lower extremity with adequate skin coverage is much easier to obtain in the child than in the adult. Coverage in most children can be effected, at least temporarily, with use of free grafts and local flaps without the use of distant flaps. Long-standing immobilization of a joint of a child or exposure of the joint of a child are not the major problems that they are in the adult. Inherent healing facility, basic circulation, and the elastic mobility of the skin in the child is better. Exposure of bone in the lower extremity in the child does not usually cause major difficulties.

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SERUM GLUTAMIC OXALACETIC TRANSAMINASE ACTIVITY IN ACUTE AND CHRONIC ALCOHOLISM

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Eighty per cent of chronic alcoholics exhibited a significant and characteristic rise in the SGO-T activity after acute alcohol intoxication without alteration in the results of the other tests of liver function. There was a rough correlation between the blood alcohol concentration and the SGO-T activity. None of the healthy volunteers developed increased SGO-T activity after ingestion of large amounts of alcohol. The ingestion of alcohol in the chronic alcoholic may lead to cellular damage that may become irreversible after a period of time, with subsequent replacement of liver parenchyma with fibrous tissue and the development of Laennec's cirrhosis.

The purpose of this paper is to present studies of serum glutamic oxalacetic transaminase (SGO-T) activity before, during, and after heavy alcohol ingestion and to correlate the changes in enzyme activity with blood alcohol level, icteric index, thymol turbidity, and serum protein levels as determined by paper electrophoresis.

A pilot study demonstrated normal SGO-T levels in hospitalized chronic alcoholics not having access to alcohol. In one patient the SGO-T activity was followed at close intervals within the first few days after he had consumed large amounts of alcohol. A striking increase of the SGO-T activity was found within the first 24 hours after the alcohol intake, while the icteric index, alkaline phosphatase level, thymol turbidity, and serum protein levels remained within normal limits.

The SGO-T activity is greatly increased in viral hepatitis but may be normal or slightly elevated in cirrhosis of the liver.[1] Experimental carbon tetrachloride poisoning in rats [1a] and virus hepatitis in mice [2] are followed by striking increases in SGO-T activity which are relatively proportional to the degree of cell damage observed at autopsy. These data suggest that the mechanism of elevation of the SGO-T activity is a release of large amounts of enzyme through the damaged liver cells, but alterations of the rate of destruction and excretion of the enzyme through the damaged liver may also to a certain extent account for the increased SGO-T level. Further experimental data are needed to elucidate this problem.

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Chronic alcoholism has been considered by many investigators to be an important contributory factor in the development of Laennec's cirrhosis, but little is known about the exact pathogenesis. Clinical observations have suggested and experimental data have demonstrated a hepatotoxic effect of alcohol which, however, can be accelerated or prevented by dietary measures.[3] The diet of the socially deranged alcoholic is usually low in protein and supposedly deficient in the so-called lipotrophic factors, such as methionine and choline. According to the prevalent theory, a relative deficiency in lipotrophic liver-protective agents may be an important pathogenic factor in the development of the alcoholic cirrhosis. Treatment of cirrhosis with these substances, however, has been without demonstrable effect.[4]

Seventy-five per cent of alcoholic patients have been shown at autopsy to have fatty livers, but only 9% had Laennec's cirrhosis.[5] This and experimental observations [6] have led to the thought that the fatty liver (steatosis) probably represents a precirrhotic stage. Punch biopsies of fatty livers before and after adequate diet was given and alcohol withdrawn have shown that steatosis of the liver is a reversible process.[7] Fatty liver in the alcoholic does not usually give rise to symptoms, and findings on liver function studies are almost always within normal limits.

Material and Methods

Thirty-nine chronic alcoholic subjects, aged 27-78 years, who had all been heavy drinkers for 10 years or more, were admitted to the hospital whenever it was obvious that they were acutely intoxicated. The majority of these patients had been under psychiatric treatment in the clinic for several months to several years and were supposed to be taking disulfiram (Antabuse). At the time of admission none showed evidence of a disulfiram-alcohol reaction. Punch biopsies of the liver were done in three of these patients.

A control series consisted of 19 patients who were inmates at a closed municipal institution for the treatment of chronic alcoholism. These patients were on management with disulfiram and had not taken alcohol for months. An additional control series of 12 healthy individuals (medical personnel) whose alcohol consumption was minimal were given 200 cc. of aquavit (45% alcohol).

Blood was withdrawn from the alcoholic patients immediately on admission (1 to 10 hours after the consumption of alcohol) for determination of blood alcohol levels, thymol turbidity, icteric index, serum protein levels (by paper electrophoresis), and SGO-T activity. These tests were repeated once or twice daily while the patients were in the hospital. The same procedures were followed with the control groups.

The SGO-T activities were determined spectrophotometrically by the method described by Henley and Pollard.[8] Our upper limit of normal of SGO-T level, as determined by this method, has been 2 mM. of pyruvic acid per milliliter of serum per hour. One millimole of pyruvic acid per milliliter per hour corresponds to 20 spectrophotometric units.[9] Four units is considered to be the upper limit of normal, for the thymol turbidity test. Icteric index determinations were done by the Meulengracht method, and values of more than 7 units were considered pathological. Widmark's method was used for blood alcohol assays, and the results were given as the average of three determinations. In our laboratory the ranges of normal for paper electrophoretic determinations are as follows: albumin, 4.17-4.89 Gm. per 100 cc.; globulin, 2.0-3.17; and globulin fractions: alpha$_1$, 0.27-0.41; alpha$_2$, 0.45-0.63; beta, 0.65-1.05; and gamma, 0.65-1.08.

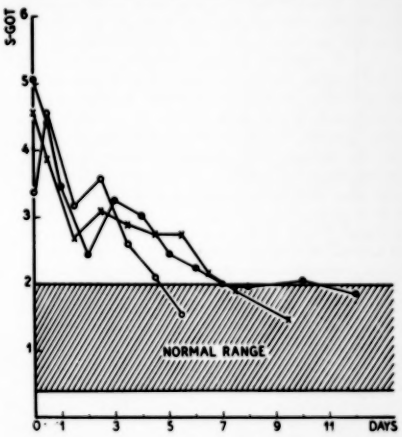

Fig. 1.–Serum glutamic oxalacetic transaminase activity after acute alcohol intoxication in three chronic alcoholics.

Results

Four patients were excluded from the alcoholic group because the results of liver function tests showed signs of "active cirrhosis" and the SGO-T showed considerable spontaneous variation. Eight patients showed normal SGO-T activities on repeated determinations. The remaining 27 patients showed elevated SGO-T activities 1 to 11 days after the acute alcohol intoxication varying between 2.18 and 10.85 mM. per milliliter per hour. The average maximum SGO-T activity of these patients was 4.1 mM. per milliliter per hour, present on the initial blood sample. Occasionally, a further

rise was observed during the first 48 hours after admission; normal values were usually encountered after three to five days. The shortest time the SGO-T level was observed to be elevated was 24 hours, and elevated activities were found as late as 11 days after admission. Figure 1 shows three typical tracings for SGO-T activity.

Eighteen patients were under observation in the hospital until normal SGO-T activities were obtained, but during their two-to-seven-day hospitalization "typical" SGO-T curves were obtained in all. Thymol turbidity and icteric index were normal on repeated determinations in the entire

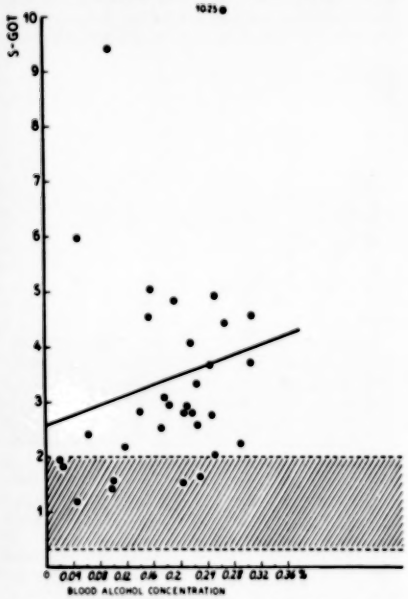

Fig. 2.—Relationship between blood alcohol concentration on admission and maximum serum glutamic oxalacetic transaminase levels in 33 chronic alcoholics. Solid line is average maximum level.

group of 35 alcoholics. The gamma globulin level, as determined by paper electrophoresis, was never found elevated; conversely, the serum globulin and particularly the gamma globulin values were frequently found lower than normal for our laboratory.

Liver biopsies were performed on three patients who showed typical SGO-T level elevations. In two cases, slight fatty infiltration was found, while in the third the biopsy was entirely normal.

The blood alcohol concentration in the 27 patients who had increased SGO-T activities after the acute alcohol intoxication averaged 0.204% (range, 0.049% and 0.308%). The eight patients who had normal SGO-T values had an average blood alcohol concentration of 0.113%, varying between 0.025% and 0.223%. A rough correlation was found between the blood alcohol concentration encountered immediately after admission and the maximum SGO-T activity (fig. 2). It must be borne in mind that the blood alcohol concentration found on admission did not always represent the maximum, as the patients were admitted at different time intervals after the alcohol intake.

In order to ascertain the direct relationship between the alcohol intake and the rise in the SGO-T activity, the SGO-T activity was followed at close intervals in a 49-year-old man after alcohol administration on two occasions during the hospital stay (fig. 3). The first spike of the tracing represents the rise in SGO-T activity after admission. The blood alcohol concentration was 0.158%. Two weeks later the patient was given 225 cc. of aqua-

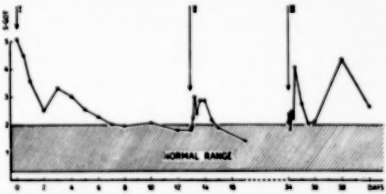

Fig. 3.—Serum glutamic oxalacetic transaminase activity in a 49-year-old chronic alcoholic: I, on admission, blood alcohol concentration 0.158 %; II, first alcohol tolerance test: 100 Gm. of alcohol given, blood alcohol concentration 0.178 %; III, second alcohol tolerance test: 135 Gm. of alcohol given, blood alcohol concentration 0.216 %.

vit (alcohol content, 100 Gm.), after which his blood alcohol concentration rose to 0.178%. A typical rise in the transaminase activity was observed in the serum, and normal values were found again after 48 hours. In another "alcohol tolerance test," after 300 cc. of aquavit (135 Gm. of alcohol) was given the blood alcohol concentration was 0.216% and the SGO-T activity was found to be more elevated this time than it was after the first test.

In another patient we had the opportunity to follow the SGO-T activity after two episodes of acute alcohol intoxication. Figure 4 shows the moderate rise in SGO-T activity after the first bout. The patient insisted on leaving the hospital after 24 hours, but 6 hours later he was readmitted in a state of severe intoxication. During the following days a considerable rise in the SGO-T activity, with a peak on the fifth day, was observed. At the time of the first admission, the blood alcohol concentration was 0.114%; on the second admis-

sion it was 0.049%. The marked and prolonged rise in SGO-T activity after the second episode, when only a moderate blood alcohol level was encountered, could be the result of a continuing insult to a liver that had not fully recovered from the prior intoxication.

Control Series.—The control series comprised 19 chronic alcoholics, inmates of a municipal institution for the treatment of chronic alcoholism, and 12 healthy volunteers. In the inmates the liver function tests (thymol turbidity, icteric index, and paper electrophoretic determinations) were normal. Eighteen of these patients showed normal SGO-T values; in one patient a slight elevation was found on the first determination (2.19 mM. per milliliter per hour), but normal values were encountered on subsequent determinations.

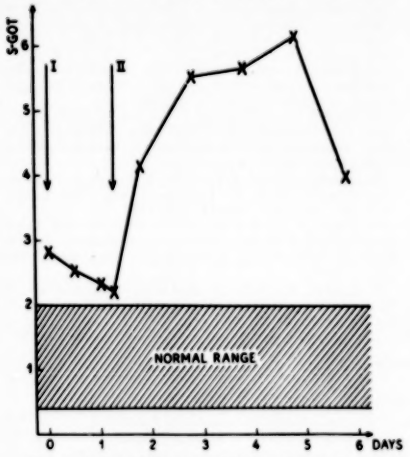

Fig. 4.—Serum glutamic oxalacetic transaminase activity in a 32-year-old chronic alcoholic after two admissions in acute intoxication: I, blood alcohol concentration 0.141%; II, blood alcohol concentration 0.049 %.

The SGO-T activity and the liver function tests in 12 healthy nonalcoholic individuals after the administration of liberal amounts of alcohol remained within normal limits. The average blood alcohol level was 0.136%, varying between 0.098 and 0.197% as compared to 0.204 and 0.113% for the alcoholic groups.

Comment

None of the chronic alcoholics in this series had clinical or biochemical evidence of hepatic disease, but 80% exhibited a significant and characteristic rise in the SGO-T activity after acute alcohol intoxication without alteration in the results of the other tests of liver function. Furthermore, there was a rough correlation between the blood alcohol concentration and the SGO-T activity. These data suggest that in this group of alcoholics the ingestion of alcohol resulted in acute liver cell damage and confirm the prior experimental evidence and clinical observations of a direct hepatotoxic effect of alcohol when administered after long periods of inadequate diet. Whether this was the result of latent, indetectable liver disease (fatty infiltration of the liver) or of deficiency of dietary substances ordinarily protecting liver cells from the effects of alcohol cannot be ascertained on the basis of our present data.

In two of three patients for whom liver biopsies were done fatty infiltration of the liver was found; in the third the liver was found to be normal. All three patients had significant increases of SGO-T activity of the same magnitude after alcohol intake, suggesting that fatty liver, per se, does not give rise to increased SGO-T activity.

The fact that the rise in SGO-T activity could be reproduced twice in a chronic alcoholic by administration of alcohol after two weeks and five weeks of adequate varied hospital diet and withdrawal of alcohol suggests the presence of subliminal liver disease as a major factor in the release of transaminase from normal liver cells as a direct reaction to the ingestion of alcohol. A final evaluation of the role of the diet cannot be given on the basis of this single observation. To clarify this further, a series of chronic alcoholics are at present being maintained on a nutritious, high-calorie, high-protein diet with massive vitamin supplements, and studies of changes in the SGO-T activity after ingestion of alcohol are being carried out at four-to-six-week intervals.

None of the healthy volunteers developed increased SGO-T activity after ingestion of large amounts of alcohol. Although their blood alcohol concentration was somewhat less than in the alcoholic group with increased SGO-T activity, this latter observation indicated that increased concentration of alcohol in the blood or metabolites does not alter the indicator system for transaminase assay ($DPNH_2$-DPN) so as to give rise to false-positive results.

It is felt that the above data may indicate that the ingestion of alcohol in the chronic alcoholic will lead to cellular damage that may become irreversible after a period of time, with subsequent replacement of liver parenchyma with fibrous tissue and the development of Laennec's cirrhosis.

Summary

Serum glutamic oxalacetic transaminase (SGO-T) activity increased in 27 of 35 patients with chronic alcoholism after acute alcohol intoxication, while thymol turbidity, the icteric index, and the serum protein levels, as determined by paper electrophoresis, remained within normal limits.

The SGO-T activity remained elevated for from two hours to 11 days after the alcohol intake but, on the average, fell to normal by the fourth day. A rough correlation was found to exist between the blood alcohol concentrations and the maximum SGO-T activities.

The rise in transaminase activity could be reproduced in the chronic alcoholic by the administration of alcohol at a time when the patient was maintained on a varied, sufficient hospital diet for five weeks. The SGO-T activities remained within normal limits for two weeks in 19 chronic alcoholics who had no access to alcohol. The SGO-T activities remained within normal limits also in 12 healthy, nonalcoholic individuals after the administration of large amounts of alcohol. These observations may indicate that alcohol has a direct hepatotoxic action on the liver of the chronic alcoholic.

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Frank Lundquist, Ph.D., of the Institute of Forensic Medicine, Copenhagen, did the blood alcohol assays.

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POCKET NEBULIZERS IN TREATMENT OF ASTHMA.—The psychologic component in cases of bronchial asthma is often referred to in medical literature. In most instances, it is highly exaggerated. However, it is often clearly evident in cases of chronic asthma in which repeated attacks of suffocation have occurred. In such cases, the patients live in a state of apprehension, always in fear of another attack. The mere presence of a nebulizer containing an appropriate medicament, which from experience they know will give them almost instant relief, may help restore their equanimity and give them the sense of security they so sorely need. The practice of allowing pocket nebulizers and the medicament to be used in them to be sold over the counter by druggists is a distressing matter. Their use definitely should be limited to the prescription by a physician who has examined his patient and feels that it would be helpful for the patient to have this therapeutic device. In many cases it may not be necessary. . . . The use of pocket nebulizers with sympathomimetic drugs for the treatment of acute attacks of asthma is efficient and generally reliable. There is no toxicity with their use, and they have few, if any, side effects. If the use of a pocket nebulizer is properly explained to a patient, it does not deter the patient from seeking investigation of the cause of the attacks and thereby securing specific and more lasting therapy. Too frequent use of pocket nebulizers can be obviated by prescribing a nebulizer which administers a measured standard dose, and by specifying to the patient under what conditions the nebulizer should be used.—M. C. Harris, Use and Abuse of Pocket Nebulizers in Treatment of Asthma, *Postgraduate Medicine*, February, 1958.

WHAT IS "THE CAUSE OF DEATH"?

Carl L. Erhardt, New York

Few physicians are familiar with the processing of death certificates in a vital statistics office to produce mortality statistics. This lack of knowledge is reflected in the often inaccurate use of such statistics, without due regard for such influences as certification habits of physicians, the concept of a single cause of death, management of nosology problems, and the classification system used. These influences have particular import in mortality from diabetes with its current high frequency of cardiac and vascular complications that may be certified as either underlying or contributory causes of death. It seems profitable, therefore, to review some of these factors to assess their part in determining the meaning of mortality statistics.

The process starts with the recording of the cause of death by the attending physician, and it is a truism that mortality statistics can reflect no more than what he reports. If we assume for the moment that the physician has thoughtfully and clearly recorded his best clinical judgment regarding the conditions that led to death and any significant pathology contributing, what then comes out in the statistics, how does it get there, and why are some manipulations necessary at times? What efforts have been, or are being, made to improve the process and the data?

The primary or underlying cause of death is defined as that condition or injury (or circumstances of the injury) that initiated the train of morbid events leading directly to death. The question sometimes arises as to which of several existing conditions has caused death. The clinician may logically say that none of the diseases singly, in a specific patient, caused death, but rather the complex of conditions. Only the physician in attendance can judge adequately which of several conditions was the most important factor in the death of the patient; yet improper completion of about 80,000 death certificates a year requires that nosologists in vital statistics offices interpret the physician's meaning. Whether the traditional concept of a single cause of death is adequate to current needs is an elemental question that would generate wide serious discussion. The major users of information on death certificates are research clinicians, pathologists, and physicians, not only those in public health but also practicing physicians with special interests. The attending physician, therefore, in completing the death certificate, is fundamentally transmitting information to his colleagues. His respect for them should be adequate incentive to do the job right. The physician must be influenced to change his attitude that the death certificate is "just paper work," that its completion is a last rite for someone no longer of clinical interest, and that it represents merely another bit of bureaucratic red tape.

Classification of Diseases

To be digestible, any mass of data must be summarized in a regular manner. Causes of death must likewise be grouped in some way to permit a view of the forest apart from the confusion of trees. The purpose of a classification of diseases is to accomplish this summarization for analytic purposes. A disease entity appears as a separate item in a classification if it is numerically frequent, if it is especially serious, or, perhaps, if it has peculiar interest for medical research. Otherwise, similar conditions are grouped. The groupings may be assembled in a number of ways: pathologically, etiologically, anatomically, or on other axes. In practice, the schema used for causes of death is a compromise between a number of such axes: etiology, anatomy, circumstances of onset, and the like.

Nomenclature of Diseases.—Much confusion exists regarding the distinction between a nomenclature and a classification, and it is important to distinguish between them at the outset.[1] As indicated previously, a classification summarizes for analytic purposes. Every disease entity, condition, or state must have a "home"—a category in which it belongs, sometimes alone, sometimes with other related conditions. A nomenclature, on the other hand, is essentially a list of approved terms for stating clinical observations in order that such terms may be uniformly used and understood. By its very nature, a nomenclature must provide a distinct and separate term for each morbid condition that can be specifically described. A nomenclature and a classification will not be confused if their respective fundamental purposes are understood.

The appropriate reference for describing diseases is the Standard Nomenclature of Diseases and Operations.[2] This universally accepted nomenclature is based on the simple principle that every disease

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has an anatomic and an etiological component. Consequently, its basic arrangement is anatomic, diseases being listed according to the major anatomic regions with the initial section covering the psychobiological unit for psychiatric diagnoses and the second scheduling the body as a whole for systemic disorders. Within each section for anatomic regions, the etiological factors affecting specific sites are arranged in uniform order. Since the system is extremely flexible, it allows for description of any condition in utmost detail. Utilization of the Standard Nomenclature by physicians can reduce the questionable terminology that sometimes appears on death certificates. Thus proper use of the nomenclature in describing diseases will aid proper use of a classification in grouping them.

History.—Attempts to classify diseases developed in remote times; recent systems originated in the early 18th century. In 1854, the first general agreement was reached on a system of classification, limited to causes of death. Modifications in this International List of Causes of Death were made at intervals. More widespread adoption of the Bertillon classification (1893) occurred, the American Public Health Association in 1898 urging its adoption throughout Canada, the United States, and Mexico and further recommending its revision every 10 years. Such revisions have, in fact, been made at approximate decennial intervals since that time. The sixth revision (1948) was retitled the International Statistical Classification of Diseases, Injuries, and Causes of Death (ISC) and comprised for the first time a combined morbidity-mortality schema, the groundwork for which had been laid as far back as 1856.[3] The seventh revision (1955), effective in the United States this year (1958), is a relatively minor modification of its predecessor.[4]

Classification Revision.—The need for regular revision of a classification of diseases is obvious if the schema is to reflect modern medicine. Identification of disease organisms and their grouping, the recognition that apparently systemic disorders represent dysfunctions of certain organs, the tracing of deficiency diseases, new knowledge of the etiology of specific diseases—all such medical advances require change in the structure of the classification to allow adequate analysis. Obviously, revisions must follow not only the discoveries but also the acceptance of the facts by the medical profession. At the same time, the system must allow for wide variation of familiarity with most recent medical advances and modern medical nomenclature. It can at best reflect the average medical sophistication, if it is to be of practical use.

Changes in the structure of the classification (and other factors) may, however, introduce differences in the statistics that obscure determination of trends for specific conditions. A major break with the past, for example, occurred with the adoption of the sixth revision of the International Statistical Classification in 1949; substantial proportionate decreases were effected in deaths ascribed to such conditions as nephritis, diabetes, and syphilis, while increases resulted for such conditions as rheumatic fever, diarrhea and enteritis, influenza, and cerebrovascular lesions.[5]

In the New York City series,[5b] for example, there were reported 52,517 deaths that had been coded according to both fifth and sixth revisions of the International Statistical Classification. Of these, 2,367 were classified as due to diabetes mellitus under the old system. Under the new system, only 1,054 of the 52,517 deaths were ascribed to this disease, a reduction of 65%. For 1,038 of the deaths, the change in procedure had no effect; they were charged to diabetes under both methods. But 16 deaths were added to the diabetes count (under old system cause of death attributed to cancer in 6 instances), and 1,329 were assigned to causes other than diabetes under the new system. The majority of the deaths transferred from diabetes to other causes were charged instead to arteriosclerotic heart disease (713), with a substantial number going to hypertensive disease (242) and cerebrovascular lesions (185). Such aberrations were caused, to some degree, by the change in the classification. But, to a major extent, they resulted from the adoption of a new method of medical certification and of the manner of selecting the primary or underlying cause of death.

Little further effect on long-term series should result from introduction of the seventh revision this year, since modifications have been deliberately limited. Some realignment of mortality within the cardiovascular-renal group may be expected however, although not of the same degree as in 1949. Hypertension and hypertensive heart disease can be expected to show some increase at the expense of arteriosclerotic heart disease. To that extent, arteriosclerotic etiology receives less emphasis in the seventh revision than in the sixth revision. The exact extent of change cannot now be determined, but seems unlikely to be radical.

Sudden breaks in long-term trends due to classification or certification changes are generally identifiable, and adjustments may be made to counteract their effects in analysis. More subtle influences derive from the dynamic state of medical science. Dissemination of new knowledge can result in more specific etiological statements that require assignment of a disease to a different category than that used for the earlier, more obscure description. Alteration of medical opinion may cause an apparent decline in one condition and contribute to the rise of another. Sudden and unattended deaths, in years past, were often ascribed to heart failure, acute indigestion, and stroke, for example; at present most of such deaths are said to be caused by coronary artery disease. Mortality from the former conditions shows little variation over recent decades, despite increases in the aged population, but

part of the rise in the death rate for arteriosclerotic heart disease (including coronary artery disease) may have been caused by this shift in diagnosis.

Selection of Primary Cause of Death

The primary or underlying cause of death is defined as that condition or injury (or circumstances of the injury) that initiated the train of morbid events leading directly to death. In populations with high mortality and short life expectancy, death is most often caused by infectious or communicable disease. Under such circumstances, the cause of death can often be expressed as a single term. As length of life increases, however, with the conquest of such diseases, aging permits the development of degenerative processes that affect many body systems. The question then arises as to which of several existing conditions caused death. The clinician may logically say that none of the diseases singly, in a specific patient, caused death, but rather the complex of conditions. But the classification does not provide for combinations of diseases in most instances. Moreover, preventive medical programs have traditionally sought information regarding the initiating factor in the disease sequence leading to death, in order that efforts toward prevention might be placed at the start of the process.

Whose Responsibility?—It has always been recognized that intimate knowledge of the individual patient and the course of the several conditions from which the patient was suffering provided the only reasonable bases for selecting a single underlying cause of death. Solely the physician in attendance, therefore, can judge adequately which of several conditions was the most important factor in the death of the patient. Consequently, death certificates formerly asked the physician to name the "primary cause" or "principal cause" and to state separately "contributory causes." But physicians were often confused by this terminology. "Primary" or "principal," intended to mean the "underlying" or initiating," disease was often interpreted to signify the terminal state instead. Moreover, different physicians interpreted the terms in varying fashion, compounding the difficulty for the vital statistics office of understanding their intents in completing the death certificates. To clarify the situation, the physician was then asked to underline the cause to which he believed the death should be ascribed in mortality tabulations, but even this method was not at all satisfactory, for few physicians troubled to underline any of the conditions on the certificates.

Need for Rules.—Because the intent of the certifying physician was frequently unclear, methods for selecting the cause of death varied from place to place. Hence, comparison of mortality statistics was hazardous. To ensure uniform selection of the underlying cause by the nosologist regardless of the manner in which the physician expressed himself, a standard procedure was devised. In the United States, the Manual of Joint Causes of Death, used for many years prior to 1949, determined precedences (or priorities). For tabulation purposes, when two or more diseases were reported on the same death certificate, reference to the manual directed which of the conditions was to be selected as the cause. A priori decisions, based on judgment as to the relative clinical severity of various diseases, generously influenced, it must be admitted, by interest in specific conditions, determined the selection. Investigations showed, fortunately, that this arbitrary procedure reflected the physician's opinion as to underlying cause in most instances.[6] However, under the method adopted in 1949, designed specifically to improve the situation, a substantial number of deaths are still subject to misclassification, as will be subsequently seen, because of continued need for arbitrary rules.

Present Method.—It was the abandonment of this arbitrary practice that had much to do with the major disturbances of trend data in 1949, for a new mechanism was then introduced to place the responsibility for selection of the underlying cause where it belongs—on the attending physician. Long experimentation in Great Britain with a medical certification form that would accomplish such a purpose led to the adoption by the World Health Organization (WHO) of an internationally recommended format modeled on the British experience; this format, used throughout the United States since 1949, is illustrated in the figure. Essentially, it provides for medical certification in two parts: the first part includes several lines for the physician to state either a single condition (for example, scarlet fever) or a pathologically or etiologically related sequence of conditions with the most recent manifestation stated first (for example, septicemia due to gangrene due to diabetes). Part II of the medical certification allows for the reporting of other significant conditions contributing to the death but not directly related to the disease last named in part I.

When the medical certification has been properly completed, the cause selected for tabulation will be the last-mentioned condition in part I of the certification. Thus, the physician determines the underlying cause of death and directs its selection by the manner in which he completes the record. For example, if the physician reports in part I: (a) coronary thrombosis due to (b) arteriosclerosis due to (c) diabetes mellitus, and leaves part II blank, the death will be charged to diabetes. On the other hand, if he completes the certification thus: I (a) coronary thrombosis due to (b) arteriosclerosis due to (c) (no entry), II diabetes mellitus, the arteriosclerotic heart disease will be considered the underlying cause of death for tabulation.

Unfortunately, despite the ease of correct reporting, in many instances it is necessary to resort to

rules for selection of the underlying cause. The physician may report a related sequence in apparently reverse order (as indicated by the probable etiological relationships or by the duration intervals stated for the various conditions in the sequence); or he may record clearly unrelated conditions in part I (for example, diabetes [due to] inguinal hernia). The nosologist in the vital statistics office has only two courses open: to query the physician, who is acutely annoyed as a result, or to decide the issue

part II left blank. The three conditions together form an etiologically related process in which diabetes was the initiating disease. However, arteriosclerosis could have led to gangrene in the absence of diabetes. The practice under circumstances where two different etiological sequences are equally possible is to accord preference to that sequence first completed. In this case, therefore, the death would be ascribed to arteriosclerosis. It might be argued that a reasonably complete se-

15. WAS DECEASED EVER IN U. S. ARMED FORCES? (Yes, no, or unknown) (If yes, give war or dates of service) | 16. SOCIAL SECURITY NO. | 17. INFORMANT

18. CAUSE OF DEATH
Enter only one cause per line for (a), (b), and (c)

*This does not mean the mode of dying, such as heart failure, asthenia, etc. It means the disease, injury, or complication which caused death.

MEDICAL CERTIFICATION

1. DISEASE OR CONDITION DIRECTLY LEADING TO DEATH* (a) _____
ANTECEDENT CAUSES
DUE TO (b) _____
Morbid conditions, if any, giving rise to the above cause (a) stating the underlying cause last.
DUE TO (c) _____

11. OTHER SIGNIFICANT CONDITIONS
Conditions contributing to the death but not related to the disease or condition causing death.

INTERVAL BETWEEN ONSET AND DEATH

19a. DATE OF OPERATION | 19b. MAJOR FINDINGS OF OPERATION | 20. AUTOPSY? YES ☐ NO ☐

21a. ACCIDENT SUICIDE HOMICIDE (Specify) | 21b. PLACE OF INJURY (e.g., in or about home, farm, factory, street, office bldg., etc.) | 21c. (CITY, TOWN, OR TOWNSHIP) (COUNTY) (STATE)

21d. TIME OF INJURY (Month) (Day) (Year) (Hour) m. | 21e. INJURY OCCURRED WHILE AT WORK ☐ NOT WHILE AT WORK ☐ | 21f. HOW DID INJURY OCCUR?

22. I hereby certify that I attended the deceased from _____, 19____, to _____, 19____, that I last saw the deceased alive on _____, 19____, and that death occurred at _____ m., from the causes and on the date stated above.

23a. SIGNATURE (Degree or title) | 23b. ADDRESS | 23c. DATE SIGNED

24a. BURIAL, CREMATION, REMOVAL (Specify) | 24b. DATE | 24c. NAME OF CEMETERY OR CREMATORY | 24d. LOCATION (City, town, or county) (State)

DATE REC'D BY LOCAL REG. | REGISTRAR'S SIGNATURE | 25. FUNERAL DIRECTOR | ADDRESS

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Medical Certification Form for Reporting Deaths

in some systematic way. Unless the physician is asked to clarify his intent in the instance cited, or if he fails to respond, death will be charged to diabetes on the reasoning that the physician must have considered that disease more important since he stated it first and that, hence, he really meant to report the inguinal hernia in part II.

The situation is not always this clear-cut. A certification may be filed with the cause of death stated as follows: I (a) gangrene due to (b) arteriosclerosis and diabetes, with part I (c) and

quence exists and that diabetes should hence be considered as the underlying cause. But in most comparable situations the three conditions mentioned cannot be considered to form an etiologically related complex even though each of those on line (b) bears an independent etiological relationship to the disease on line (a). The rule therefore instructs the nosologist to select the first condition mentioned on line (b) that completes a logical sequence when such anomalous reports are received.

The rules that guide the nosologist in such situations have logic in them, but no rules can adequately substitute for an unambiguous, clear statement by the physician. It has been estimated that these arbitrary procedures may result in the classification of as many as 5% of the deaths to conditions other than those which the physician intended to indicate as the underlying cause.[7] This means improper classification of more than 80,000 deaths each year in the United States—more than the entire number usually occurring in the city of New York in a year! Simple attention to proper completion of the death certificate could correct this error.

Measures to Insure Uniformity

Although general rules for selection of the underlying cause of death have been established in connection with the classification itself,[8] the National Office of Vital Statistics of the Public Health Service acts as the final authority to assure uniform treatment throughout the United States of certifications that are apparently improperly completed or contain peculiarities unique to this country. This office distributes to all vital statistics offices, and to others engaged in cause of death coding, copies of the instruction manual prepared primarily for its staff.[9] The instructions derive from questions arising in coding causes of death as reported on certificates transmitted from every state and territory. When the same question has been noted a specific minimum number of times (to assure that it is not unique), a decision is made in consultation with clinicians as to how the question should be resolved to reflect the probable intent of the certifying physician. The question may then be found to be a special case of an existing rule of procedure, or, if necessary, a new rule will be established so that all similar certifications will be coded alike. Obviously, the lay coding staff must be well versed in anatomy, physiology, pathology, and etiology for this type of work. The distribution of the instruction manual throughout the country encourages uniform treatment of similar certifications in each of the agencies processing death records.

As a routine training measure for technicians, the National Office of Vital Statistics also publishes a four-page release entitled "Nosology Guidelines." Each month a specific aspect of mortality-cause coding is discussed in detail; in addition a series of medical certifications are presented as examples of difficult coding problems with their solution and an explanation for each one. More formal training in cause of death classification is provided by teams of instructors from the national office, particularly in advance of the introduction of revisions of the classification. Such "training institutes" are held in various cities so that personnel of all agencies may participate. The courses, usually of a week's duration, are designed not only for beginners but also for experienced coders to give more intensive instruction to supervisory personnel who must in turn train additional staff at the state and local level.

Other organizations are also active in these efforts to maintain comparability and to make the product more useful. The Public Health Conference on Records and Statistics, through a standing committee on mortality statistics, carries on continuous investigations to improve procedures, to establish exactly what physicians mean by certain terms they use, and to seek new approaches. *Ad hoc* committees of the American Public Health Association (APHA) and of the American Association of Registration Executives address themselves to both specific and general questions regarding mortality statistics as they arise. The most recent report, prepared by a committee of the statistics section of the APHA, discusses current problems in mortality statistics.[10] The National Committee on Vital and Health Statistics also directs investigations into problems related to classification and other aspects of mortality and fetal death statistics, as will be cited later. Comparable groups in other countries are similarly engaged; the efforts to improve every step, from initial reporting by the physician to final result in tabulations, are universal.

As an international health agency interested in comparability of mortality statistics from country to country, the World Health Organization publishes in many languages instructions to physicians in the proper completion of the medical certification, recognizing the prime importance of thoughtful accuracy in the basic document.[11] Discussions involving coding, tabulating, and interpreting data are also published.[12] Specifically for the clarification of problems connected with these procedures as they occur throughout the world, as well as to investigate methodological devices, WHO has also established a Center for the Classification of Diseases, which is attached to the General Register Office of Great Britain.

Multiple Causation of Death

It is obvious from the discussion that we have made progress in one direction: the person in the "know," the attending physician, has the opportunity to determine the cause to which the death will be charged in single-cause tabulations.

In common with many statistical series, mortality data are limited by their very nature; they refer to the dead rather than to the living population. For fatal illness with a short course, the facts about the dead may be extremely useful approximations of those facts about the living with a specific disease. But for most diseases characterized by a lengthy course, the use of mortality statistics for estimating morbidity or for assessing the characteristics of persons with such diseases may be quite misleading. The frequency of concurrent diseases, especially among the aged, further complicates interpretations. Hence, we are far from satisfying medical needs for morbidity or mortality information. For many purposes it may be sufficient to

know, for example, that, as reported by physicians, diabetes was the major factor in a given number of deaths. For other purposes, however, it would be useful to know how many persons had diabetes at the time of death, even though many of them died of other underlying causes. Even more useful would be the knowledge as to how many of those with diabetes exhibited vascular or renal damage.

Multiple Cause Tabulations.—Information on the association between reported diagnoses can be obtained, within limitations, from the present type of medical certification by tabulating all the conditions mentioned by the physician. However, the preparation of multiple-cause tabulations in a vital statistics office is a heroic undertaking. The task of coding many conditions (and some death certificates in New York City now contain as many as seven distinct diagnoses) is time-consuming. Moreover, questions arise as to what constitutes a distinct diagnosis, that is, should all clinical manifestations of disease processes be coded or not? If septicemia, gangrene, and diabetes are all reported, for instance, should all three be coded, or only the major condition?

Although multiple coding takes time, it is manageable; determination can also be made, with clinical and research advice, as to what constitutes a distinct diagnosis for tabulating multiple diagnoses. But then tabulating problems come to the fore. How are the data to be managed to allow intelligent interpretation? Simple tallies of the number of times each condition was reported could easily be prepared. Then the proportion of deaths in which each was a factor could readily be calculated, as Treloar [13] has recommended. For example, among deaths of persons 65 or more years of age in New York City in January, 1954, 8.7% were ascribed to cerebrovascular lesions. But multiple-cause tabulations indicated that a minmum of 17.1% had suffered such attacks prior to death. Similarly, 2.6% of these deaths of the aged were charged to diabetes, but diabetes was reported as a factor in 7.2%.

Without great difficulty it could be determined also how frequently diabetes occurred on the records together with gangrene, hypertension, arteriosclerosis, or chronic nephritis. But the feasibility of cumbersome four-dimensional or five-dimensional tables to show joint frequencies of some or all of these combinations appears remote. For any single major cause the problem may not be insurmountable, but the vital statistics office must serve many interests. The preparation of such tabulations for a multiplicity of diseases becomes gargantuan; the possibility of their regular analysis is well-nigh unthinkable.

Limitations.—Despite these difficulties, the interest to be served might warrant the effort, perhaps at lengthy intervals, as special studies. But some genuine scepticism would be appropriate for any conclusions that might be drawn. It was initially pointed out in this paper that the validity of mortality statistics depends on the completeness and accuracy of the reporting of diagnoses by the attending physician. The value of multiple cause tabulations depends on the extent to which the physicians report associated and contributory conditions. While some physicians report as many as seven diagnoses for a decreased patient, others record a single cause, even for an aged person.

A recent review of a small sample of death records with the attending physician revealed, for example, that hypertension is often omitted as a factor of consequence. The physician may have concluded, under our present system, that hypertension was not significant and hence omitted it. But such omissions in attempts to investigate associations between diseases might have serious import.

Another source of deficiency may lie in the reporting of about one-fourth of all deaths by the medical examiner, who does not have a complete clinical history of the patient and who did not know the person when he was alive. Citing New York City data, Lew [14] points out that almost 15% of deaths ascribed to arteriosclerotic heart disease and 44% of those classified as due to coronary artery disease were certified by the medical examiner but that autopsy verification was available for only 4 and 8% respectively. Even among deaths from these conditions certified by private physicians, the proportion in which the diagnosis is confirmed by autopsy is well under 10%.

The facts derived from multiple-cause tabulations under present circumstances, therefore, will represent a select group of deceased persons, those whom the signatory physician knew well and for whom he reported all significant pathology. But there is no convenient way of segregating this select group for intensive study. Where multiple-cause tabulations are currently attempted, they represent to a major degree methodological experimentation and the hope that knowledgeable, critical analysis will suggest special studies.

The Future

The spectacular decline of infectious and communicable diseases as causes of death have left us as major causes those that affect the two ends of the age scale—infant and aged—and accidents. Although it is recognized that mortality statistics regarding chronic diseases will often give biased information about what we actually seek—morbidity—it must be equally recognized that mortality statistics still serve, and for many years will continue to serve, useful purposes. Such data are continuously criticized, sometimes with justification, sometimes through misunderstanding. But their wide use is a matter of necessity. Reliable morbidity data that we might prefer for specific purposes are rarely available. The established vital statistics system is, moreover, a convenient mechanism for obtaining information about the entire population. Critics can effectively improve the situation by

using the material with good judgment as to its limitations, by joining in attempts to improve the basic data, and by encouraging the efforts toward betterment of classification and tabulating procedures. Since mortality data are, and will be, widely used, it behooves us to give thought to methods for their improvement.

Whether the traditional concept of a single cause of death is adequate to current needs is an elemental question that would generate wide serious discussion. Moriyama [7] has expressed the need for such discussion in his description of the development of the present concept, while Treloar [13] has recommended that the death record be designed to elicit fully the disease states existing at the time of death and that attempts to ascribe each death to a single cause be abandoned.

The sixth revision of the ISC, as previously mentioned, combined for the first time a morbidity and a mortality classification to provide a common denominator for mortality statistics and the ever-increasing number of morbidity studies. The main purpose of publishing a seventh revision at this time is to adjust the time for issuance of revisions to the midddle of a decade; the next revision is expected in 1965. The aim is to have the classification and all its appurtenant procedures well established in any decade by the time a census is taken. Such timing permits detailed mortality analyses according to population characteristics, such as age and sex, under the best circumstances, with stability in the tabulations when census data are available for construction of valid rates.

The intervening years until 1965 can profitably be used for studies directed toward suggestions for substantive revisions in the classification that will lead to more meaningful mortality statistics. That section of the classification dealing with the cardiovascular system, for example, is a compromise of anatomic, etiological, and pathological expressions. No clear presentation of any one of these aspects is possible; combined etiologies likewise cannot be dealt with, nor can anatomic involvement be uniformly specified. It often happens, for example, that hypertensive heart disease and arteriosclerosis are reported on the same certificate. Up to this year, such deaths have been charged to the former condition. But, if hypertensive heart disease and arteriosclerotic heart disease were reported together, the death has been charged to the latter. With the seventh revision of the ISC, allocation will depend more on the specific wording of the physician's certification. In any case, it may well be questioned whether the same disease complex may not be operating in both situations.

On the other hand, a cerebrovascular accident is classified on an anatomic basis without reference to etiology at all, unless the physician specifically states that the lesion was caused by "malignant hypertension." In such a circumstance, death will be charged to hypertension. If "hypertension," otherwise unqualified as to activity, is stated as underlying etiology, it will be ignored and the death will be ascribed to the cerebrovascular lesion. Some recommendations have already been made for improvement of the cardiovascular classification.[14] It is not too early for such proposals to be reviewed in a constructively critical manner in order that they may be amended, extended, or otherwise modified to permit the most productive use of mortality statistics on cardiovascular disorders.

The rise of interest in perinatal mortality has made cause classification of fetal and infant deaths by separate and uncoordinated systems an anachronism. A subcommittee of the National Committee on Vital and Health Statistics is presently drafting a comprehensive group of disease categories that will effectively summarize those conditions that are peculiar to fetal and infant loss. These proposals will likewise have to be carefully examined, particularly by obstetricians, pediatricians, and pathologists. Furthermore, actual experimentation in their use will be required in a few vital statistics offices, a number of hospitals, and by several pathologists to assure their practicability and adequacy.

Expert recasting of the sections of the ISC dealing with neoplasms and with psychobiological disturbances is needed to satisfy critics of their deficiencies. Other sections of the code can also undoubtedly be improved. Disease-complex type of categories may be suitable in other parts of the classification schema, just as they have been suggested for the cardiovascular sections. Interest in research, the aging of the population, and increased frequency of concurrent but separate degenerative processes may signify need for rather broad use of combinations of disease complexes in lieu of multiple-cause tabulation of mortality data.

Finally, in some way, the physician must be influenced to change his attitude that the death certificate is "just paper work," that its completion is a last rite for someone no longer of clinical interest, that it represents merely another bit of bureaucratic red tape. The vital statistics office in any locality has proved to be for many physicians one vast "record room" where they have been able to obtain community-wide information for epidemiologic research in such widely separate areas as amaurotic familial idiocy (Tay-Sachs disease) and leukemia. The same source is tapped for end-results of specific therapy for cancer and of surgical or other treatment of many additional diseases. The major users of information on death certificates are physicians, not alone those in public health, but research clinicians, pathologists, and practicing physicians with special interests. The attending physician, therefore, in completing the death certificate, is fundamentally transmitting information to his colleagues. His respect for them should be adequate incentive to do the job right.

No research carelessly, haphazardly, thoughtlessly done is worth credence. Obervations compiled by

a clinician or other scientist who recorded what seemed "acceptable" rather than what he actually observed would contribute little to human knowledge. In similar fashion, the worth of mortality statistics depends basically on the validity, or truth, if you will, of the cause of death recorded by the physician. Much is made of the discrepancies often noted between clinical and autopsy diagnoses. Although such discrepancies are significant for individual patients, they do not materially affect many statistical distributions because there are in large measure compensating errors among diseases. Moreover, we should not expect mortality statistics to be better than diagnostic ability; the physician can relate no more in describing the cause of death than he knew in treating the patient.

Too often, however, the physician admits that the cause of death as stated represented merely what he "knew the health department would accept." In the final analysis, the health department will accept whatever the physician reports, provided it makes sense, represents a reasonable diagnostic statement, and contains enough information to allow its classification as a cause of death. When the cause of death is questioned by a health department representative, it does not mean that the physician's judgment is being impeached by someone who never saw the patient. A query merely means that the physician has either failed to express himself adequately or has omitted information essential for proper classification.

Perhaps the best proposition the physician might have in mind when he records the cause of death is this: Suppose I had been treating this patient for a number of years, but because of circumstances another physician was in attendance when the patient died. How should the attending physician complete this death certificate best to inform me (for follow-up of my patients, say) of the facts at the time of death in view of the patient's history and course? What was the train of morbid events that led to death, traced back from the final manifestation to the originating disease? What other conditions, apart from this sequence, were significant by increasing stress on this patient? Such a straightforward statement, thoughtfully prepared from knowledge of the patient and of his history, is the cause of death as it should be summarized on the death certificate.

Summary

Mortality statistics have many useful purposes. They are, however, limited by their nature; no more should be expected of them than they are capable of producing. Continuous efforts are made to improve the accuracy and usefulness of mortality data. Physicians are encouraged to report adequately their best clinical judgment; they are led to select the cause of death for tabulation purposes by the arrangement of the medical certification form. Many groups, local, national, and international, are always seeking methods of improving the value of mortality statistics by experimenting with classification changes, new procedures, and different types of tabulations. Basically, the reporting physician determines the validity of mortality statistics; his thoughtful attention to this major role will aid his community and his colleagues.

125 Worth St. (13).

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INDICATIONS AND CONTRAINDICATIONS FOR TRACHEAL FENESTRATION

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Tracheal fenestration is a surgical procedure that results in a firmly epithelialized mucocutaneous opening into the trachea, provided with lip-like valves that can act like a closing mechanism. It obviates the use of a metal cannula, and the naked opening admits semirigid catheters of sufficiently wide bore to permit effective suction for the removal of bronchial secretions in severe forms of pulmonary disease. The critical factor in the evolution of such disease is not the quantity of secretions but a reduced pulmonary reserve and a failure of the cough-mechanism. The effects of aspiration extend beyond the immediate relief from discomfort and asphyxia; often it is followed by continued improvement so that the frequency of aspirations becomes less and exercise tolerance improves. All patients eventually learn to perform the catheterizations themselves. The flaps of the fenestra permit little escape of air, and by applying suitable pressure to the flaps the patient can cough and expectorate by mouth normally. Indiscriminate use of tracheal fenestration must be avoided. It should not be used merely as a short-cut treatment for profuse cough and expectoration, nor should it be used as a substitute for operation in pulmonary suppuration.

In a preliminary report we recently introduced a new method of treatment of pulmonary insufficiency by a procedure to which we gave the name tracheal fenestration.[1] Already an unusual interest has been shown in this apparently simple surgical procedure enabling patients to practice on themselves suctioning from the depth of the airways. On superficial view this procedure appears to be merely a modified tracheostomy made for the sole purpose of bronchial aspirations in patients with inadequate expectoration. There is therefore a danger of its indiscriminate use as a short cut in treatment of all patients having excessive bronchial secretions, regardless of the underlying pulmonary disease.

For reasons discussed in our recent publication, we proposed tracheal fenestration as a treatment of pulmonary insufficiency. We emphasized that no final conclusions could as yet be reached regarding its effectiveness, nor could we adequately explain its mode of action in relieving critical dyspnea in patients with scant secretions. This, as well as the indications for the procedure, remains to be clarified through further studies in a variety of far-advanced chronic pulmonary diseases.

Lest this method of treatment become discredited through misuse, it seemed to us essential that we further discuss the present status of its indications. This can best be done through a brief review of its evolution and of the clinical experience from which this procedure was evolved and through our interpretation of its possible mode of action.

Evolution of Tracheal Fenestration

The use of tracheal fenestration evolved from years of clinical observations in the treatment of patients suffering from pulmonary insufficiency. Our experience included patients in whom tracheostomy was performed as an emergency measure, because it seemed apparent that if the airways could be kept clear the patients might be tided over a critical period. It has been a long known fact that the lives of many patients under such conditions may so be significantly prolonged. It is also well known that at such periods of critical pulmonary insufficiency tracheostomy may be a heroic measure of double-edged potentialities which may even precipitate fatal cardiopulmonary failure.[2] Furthermore, conventional tracheostomy with metal cannula affords only temporary relief. Frequent catheterization and vigorous aspiration by way of metal cannula soon becomes troublesome due to rough handling involved by frequent to-and-fro movements of catheters. The granulating stoma causes too much pain, frequent bleeding, and local infections, all too often forcing early withdrawal of the cannula and closure of the stoma. Last but not least tracheostomy is at best only a temporary measure which does not answer the purpose in the presence of pulmonary insufficiency which is permanent.

Our experience indicated the need for a modified tracheostomy to meet certain requirements, namely, one that obviates the use of a metal cannula, that will remain permanent and yet permit opening and closing at will, that will admit semirigid catheters of wide bore to permit effective suction, and that can endure much abuse as well as resist infection.

These requirements obviously called for a firmly epithelialized mucocutaneous opening into the trachea, provided with lip-like valves that could act as a closing mechanism. Accordingly, we initiated animal experimentation in which we ob-

tained the surgical collaboration of Dr. E. E. Rockey. Out of these experiments was evolved the procedure described as tracheal fenestration.[3] This procedure, which, as will be shown later, has its pros and cons, has met the above requirements quite satisfactorily in a limited number of patients on whom it has been recently performed. (All fenestration operations were performed by Dr. Rockey.)

Clinical Observations on Effects of Aspirations with Tracheostomy

Clinically a most unexpected feature was relief from pulmonary disability which frequent aspirations brought to patients who previously had had little cough and scant expectoration. This effect seemed all the more paradoxical since it occurred in spite of a marked increase of secretions aspirated by catheterization after tracheostomy, yet this result was so striking that it led us to the conclusion that a change from a dry to a wet state of the lungs was the clue to the effectiveness of treatment. This effect seemed to be confirmed also by the observation that immediately postoperatively, when catheterization and suctioning was being performed by way of the conventional tracheostomy opening, relief of symptoms appeared proportionate to the quantity of secretions aspirated. Also frequent aspirations appeared to be an important factor in the treatment. All of this naturally suggested that aspiration of excessive secretions should be the primary goal and purpose and that the main effect of tracheostomy is to make feasible more efficient mechanical removal of bronchial secretional obstructions. The mode of action of this treatment would then be fully explained by more efficient ventilation. Holding this belief, one would naturally conclude that accumulation of bronchial secretions is the sole indication for tracheal fenestration. To explain the favorable effect in patients with scant expectoration, it is therefore necessary to assume that prolonged accumulation of bronchial secretions is the cause of pulmonary disability in these cases and that there is no such condition as so-called dry emphysema.

However, from our observations we are convinced that the marked increase in aspirated secretions is the effect of the procedure itself and that much hypersecretion is freshly induced by frequent intubations and strong suctioning, which invariably cause severe coughing. Last but not least the effect of the intervention on the trachea by the creation of two openings must also be included. As will be shown later there is reason to believe that increased fluid filtration and hypersecretion in the depth of the lungs may itself be the most important factor in the effectiveness of the treatment. Equally important is maintenance of a steady elimination by suctioning to keep pace with the increased filtration and secretion. Significantly, by the time the tracheal fenestration has healed sufficiently so as to permit catheterization, the quantity of aspirated secretions is greatly reduced, yet the patients continue to improve and their exercise tolerance increases in reciprocal proportion to the secretions produced. The clinical observations just described can best be explained by the relationship between bronchial secretions and pulmonary insufficiency, a subject that we have already discussed in recent publications and will only briefly touch on here.

Relationship Between Secretions and Pulmonary Reserve

It is a clinical fact that patients with the most severe and diffuse forms of pulmonary emphysema cough and expectorate very little. Conversely, patients with extensive bronchitis and bronchiectasis with much expectoration usually show mild emphysematous changes. We described this as incompatibility between extensive diffuse emphysema and bronchitis with copious expectoration.[4] Experience has convinced us that, on the one hand, patients with severe emphysema tolerate with difficulty the complication of bronchitis with excessive secretions and that, vice versa, patients with extensive bronchitis and profuse secretions cannot tolerate overt emphysematous changes in the lungs. Combinations of emphysema with bronchitis usually fluctuate between these two extremes of much emphysema with little bronchitis and much bronchitis with little emphysema. The severity of emphysema determines the extent of bronchitis, and conversely the extent of the latter determines the severity of emphysema compatible with life.

Clinical experience has convinced us that pulmonary reserve and not quantity of secretions is the critical factor in the evolution of chronic pulmonary diseases. As a rule patients have little difficulty in expectorating even enormous quantities of secretions from their airways when their reserve of functioning lung parenchyma is adequate. Only when the pulmonary reserve becomes inadequate and the lungs begin to show signs of emphysematous overdistention do they begin to suffer from progressive "cough failure" with insufficient expectoration and dyspnea. Naturally, with equally low pulmonary reserves patients with large amounts of secretions are apt to develop "cough failure" sooner than patients with scant secretions.

Recently we pointed to clinical experience showing that in severe emphysema with almost complete lack of secretions drugs which bring about return of secretions or even their temporary increase often afford relief from dyspnea, just as in asthma relief from an attack is often marked by an outpouring of secretions. Likewise in tracheostomy clinical experience indicates that relief from dyspnea is associated

with marked increase of aspirated secretions, which occurs particularly in the early postoperative days at the beginning of catheterization. Change from a state of little or no secretions preoperatively to that of profuse secretions aspirated postoperatively is so marked as to have suggested that one is dealing with a change from dry to wet emphysema. That this excess of secretions could have long remained accumulated in the emphysematous lungs is of course inconceivable. Furthermore there is no obvious reason why dyspnea should be less with wet than with so-called dry emphysema.

Mode of Action of Bronchial Aspirations in Pulmonary Insufficiency

Change from a dry to wet state of the lungs is a remarkable phenomenon which may provide the answer to the relief obtained with tracheal fenestration from the dyspnea of pulmonary insufficiency. When this answer is known, it may well shed light on the problem of pulmonary insufficiency itself. It is possible that this new method of treatment can open up new approaches to the study of this complex problem.

Admittedly we have no definite answer to the question, but we should like to refer to some pertinent considerations, albeit theoretical, previously mentioned by us in discussions of emphysema.[5]

The structural and functional integrity of the pulmonary parenchyma is conditioned upon the normal regulation of blood perfusion in the complex capillary bed of the bronchioles and alveoli from the double blood supply of pulmonary and bronchial arterioles. Bronchiolitis with secretion of tenacious mucus plugging the terminal airways is characteristic of asthma as well as of emphysema, indicating disturbance in the bronchioloalveolar circulation and in the fluid filtration which normally acts to flush out the bronchioloalveolar spaces. This fluid filtered out from alveolar capillaries is known to have the singular mucolytic power required for the normal self-cleansing of the terminal airways of the lungs.[3] Our experience suggests that this fluid presumably derived from the alveolar capillaries in increased amounts after vigorous suctioning possibly also has marked bactericidal power. We say this because even heavy purulent sputum changes within 48 hours after suctioning has begun into the same type of viscid but clear whitish secretion that is aspirated at that period in practically all patients.

On the basis of these considerations it is our assumption that frequent catheterization with powerful suctioning in the depth of the lungs probably acts by way of correcting the pressure levels in the flow of blood and air. This could reestablish functional integrity in the bronchioloalveolar spaces and structures, and as normal circulation and filtration returns there is an increased circulation of fluid with improved self-cleansing. The latter then enables the lungs to recover the function of all available air spaces and operate with these at full compensatory capacity.

In our preliminary report we mentioned untrapping of trapped air behind bronchiolar obstructions as a possible factor. This was suggested to us by long-range observations of patients whose lives were greatly prolonged by persistent conventional tracheostomy in spite of low pulmonary reserve. These patients used catheterization as a means of relieving a sensation of chest tightness when they could no longer aspirate secretions. Watching these patients suggested to us that strong air currents were created in the depth of the lungs.

Finally, a brief remark is in place here on the question of the effect of reduced dead space. We doubt that this is a significant factor. After removal of the tracheal cannula and closure of the tracheostomy opening, patients with tracheal fenestra tell us that they are not aware of any significant leakage of air on breathing. In inspiration the flaps are drawn rather tight. On strong expiration and particularly on coughing there is escape of air and moisture unless counterpressure is exerted on the flaps. When this is done the patients can cough and expectorate by mouth normally. With the flaps closed the dead space is not reduced, yet patients continue to improve.

Problem of Indications

It should be obvious from the foregoing that the exact indications for tracheal fenestration must remain problematic until its mode of action is fully understood. In the meantime the indications will differ according to concepts about its purpose. If it were to be used merely as a more effective method of elimination of excessive bronchial secretions, then all forms of bronchopulmonary suppuration would come within the purview of its indications. Indeed practically all patients with bronchiectasis and even bronchitis with profuse secretions would then be considered candidates for this treatment.

However, we are convinced that, important as elimination of excessive secretions is, it should not be considered the sole purpose. This method of treatment is, we believe, not indicated in bronchopulmonary suppuration except where there is associated emphysema with "cough-failure" and other manifestations of pulmonary insufficiency. As it improves the pulmonary function and as it controls the bronchopulmonary infection with the aid of antibiotics, the excessive secretions will diminish and the patients will be greatly relieved. In fact the favorable results of this treatment are obtained apace with progressively decreasing need for catheterization as the quantity of secretions declines. On the other hand there is reason to believe that this method of treatment will not solve the problem

where continuous production of large quantities of purulent secretions persists, requiring continued and frequent catheterization indefinitely.

Tracheal fenestration is not the indicated treatment for localized bronchiectasis. As before, this generally requires resectional surgery. When the disease is bilaterally widespread and complicated by emphysema with difficult cough and expectoration, then tracheal fenestration may be expected to ease and prolong the life of the patient. In chronic bronchitis, recurrent infections often greatly increase the quantity of secretions and so precipitate temporary insufficiency of cough with expectoration. These acute intercurrent attacks usually respond to such modern methods of conservative therapy as the use of antibiotics, postural drainage, expectorants, bronchodilators, and detergent inhalants. Under these conditions, tracheal fenestration would be unwarranted unless permanent pulmonary insufficiency is also present.

Emphysema is associated with bronchiolitis,[5] but frequently there is also complicating infection of the central bronchi. Then the more severe the emphysema the more embarrassing becomes even minimal increase in the amounts of secretions in the airways. The latter can become incompatible with life, and therefore radical and permanent measures are called for. This method of treatment is indicated here primarily because of irreversible pulmonary insufficiency. Efficient prompt removal of even small amounts of secretion becomes a matter of vital importance only because of the associated pulmonary insufficiency. In our preliminary report we have emphasized the fact that in patients with low pulmonary reserve, even trivial respiratory infections, temporarily increasing bronchial secretions, may often cause cough-failure and precipitate attacks of pulmonary insufficiency. The sequence of events by which this may progress to fatal pulmonary hypoventilation has been recently discussed by us.[1] These clinical observations have already led thoracic surgeons to resort to tracheostomy to make feasible vitally needed radical operations (lobectomies or pneumonectomies) for a variety of pulmonary diseases in patients with low pulmonary reserve.[6] Even more frequently tracheostomy has been resorted to in order to tide patients with low pulmonary reserve over periods of pulmonary insufficiency, for example, patients with thoracoplasty. It is probable that in many such patients tracheal fenestration may in the future replace tracheostomy.

Although this is a surgical procedure it is the internist who should establish its indications by all available clinical and laboratory findings including clinical estimates of pulmonary reserve which can best be learned by long-range observations of patients. Pulmonary function studies will be necessary in many instances for more exact estimation of pulmonary reserve. For reasons to be discussed in the future it seems to us that maximal diffusing capacity determinations will perhaps best serve this purpose. This should help us to identify the cases of severe bronchitis with mild emphysema that are temporarily aggravated by periodic flare-up of the bronchitic infection and to separate these from cases of severe emphysema with bronchiolitis that are bound to progress to pulmonary insufficiency. Cardiopulmonary function studies will be required in a considerable number of patients to ascertain the role played by manifestations of cor pulmonale in the clinical picture and to determine how far the latter may still be reversible by this method of treatment. It is yet to be determined at what stage of its development cor pulmonale contraindicates tracheal fenestration. One patient with cor pulmonale of advanced degree and long standing not only tolerated the procedure well but seems to have benefited remarkably.

Pros and Cons of Tracheal Fenestration

The advantages of tracheal fenestration should be obvious from the foregoing. In our long experience with the treatment of critical pulmonary insufficiency by methods now available, we have rarely observed equal amelioration of symptoms. This is all the more remarkable since, in the cases we were so far able to follow, no significant changes in the pulmonary roentgenographic features could be demonstrated.

A disadvantage of this treatment is that it requires two simultaneous tracheal openings. A considerable proportion of patients with increased depth of the chest due to emphysema have short necks and backward displacement of the trachea so as to make the operation a formidable procedure. This is particularly so because of the state of severe pulmonary insufficiency in which these patients usually have to be operated on. In the animal experiments we aimed at a single opening protected by plastic material. However the frequency of catheterizations in the earliest postoperative period interfered with the healing of the tissues. Notwithstanding these now apparently insurmountable difficulties, we believe that surgeons will eventually come up with a method that requires only a single opening.

The question has been raised as to why it is necessary to resort to such a cumbersome operative procedure when a simple tracheostomy has in the past often accomplished essentially the same results. We would stress its permanence as the great advantage of tracheal fenestration. This makes it conveniently available at all times to those patients who are subject to recurrence of attacks, requiring emergency tracheostomy. This should also prove of great advantage in patients with paralyzed chests of any origin (due to poliomyelitis, for example) where there is also disturbed lung function and difficulty in bringing up secretions.

Conclusions

The indications and contraindications of tracheal fenestration still remain to be clarified by future experience in a large number of patients so treated and observed over longer periods. In the meantime decision for operation must be based on long-range clinical study of patients with assessment of their pulmonary reserve, often including functional tests. Chronic bronchopulmonary diseases with excessive bronchial secretions are by themselves not to be considered indications for this method of treatment unless they are associated with pulmonary insufficiency of irreversible degree. Until more is known about the procedure and its potentialities, indiscriminate use of tracheal fenestration is to be cautioned against.

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CLINICAL NOTES

CLINICAL USE OF ESTROGEN IN UTERINE PROLAPSE

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This report represents the findings in four patients with marked uterine procidentia who were treated nonsurgically with rather dramatic results: the reduction of uterine hernia after the oral and parenteral administration of estrogenic hormones.

Although uterine prolapse has been described in the newborn infant and in the nulliparous woman, it is most generally observed in the older multipara whose tissues have shown signs of loss of resiliency, as has been observed by Wilson.[1] Mengert [2] has rather conclusively pointed out anatomically that the bifid cardinal ligaments are the sole means of support in maintaining the uterus within its normal gynecologic confines. He has shown experimentally that only when the cardinal ligaments were cut, regardless of what other structures were intact, was there any appreciable descensus. The etiological factor, or factors, causing a change in the normal supporting mechanism of the cardinal ligaments is at present unknown, although many have theorized as to its cause. It has generally been an accepted fact that congenitally poor, inept, and inelastic supporting structures, found usually in most hernias, constitute the main reason for their production. A review follows of four patients, all of whom were several years past the menopause and had been complaining of uterine descensus for varying periods of time.

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Report of Cases

Case 1.—A 66-year-old woman, referred because of her discomfort while ambulatory, stated that she felt that her "pelvic organs were all falling out." She had undergone the menopause 15 years previously and for the last 4 or 5 years had worn a pessary to support her uterus. At the time of examination, the pessary had been removed because of vaginal irritation.

Pelvic examination revealed a uterine prolapse, which brought the small eroded cervix out of the introitus on straining. The uterine corpus was atrophic but otherwise was not abnormal. A cystocele and a rectocele of appreciable size existed in conjunction with the prolapse. One child, aged 35 years at the time of writing, had been delivered uneventfully, and the postpartum course had been also uneventful. Slides prepared with used of Papanicolaou's stain revealed a low estrogenic level, no tumor cells, and very slight keratinization of any of the cells. The patient was advised to have the procidentia corrected by means of a vaginal plastic operation, to which she agreed. Surgery had to be postponed, because it was necessary for her to care for her sister, who was quite ill in a distant city. Her initial visit was in September, 1957. She returned after the death of her sister, complaining severely of the prolapse and other menopausal symptoms, such as hot flashes. Pelvic examination on Jan. 17, 1958, revealed the physical findings to be identical to those seen on her first visit, but with the addition of an excoriation of the skin about the vulva and the anus. It was thought wise to treat this patient for her menopausal symptoms prior to surgery. She was given conjugated estrogenic substances (Premarin), one 2.5-mg. tablet daily, and 20,000 units of estrone hypodermically. She returned on Jan. 24th, stating that her prolapse had disappeared and that her menopausal symptoms had left. Her pelvis was examined on Jan. 31st, and her statement of the disappearance of the uterine procidentia was corroborated, although a cystocele was still

present to a lesser degree. The oral dosage of conjugated estrogenic substances was continued until April 11, 1958, at which time administration of conjugated estrogenic substances, 2.5 mg. every other day, was suggested. At the time of writing (May 30, 1958), there has been no return of her uterine procidentia.

Case 2.—A 65-year-old woman had worn a "doughnut" type of pessary for six or seven years because of marked uterine procidentia. Two children, aged 42 and 35 years at the time of writing, had been normal deliveries, and her postpartum courses had been normal. Her menopause had been at the age of 57. She had been a hospital patient on eight different occasions because of severe coronary heart disease. Pelvic examination on March 12, 1958, revealed a complete procidentia, a small atrophic uterine corpus, and an ulcerated cervix. Slides prepared with use of Papanicolaou's stain showed an over-all pattern of low estrogenic level, no tumor cells and very few keratinized cells. Inasmuch as this patient was such a poor surgical risk, it was thought best to treat her conservatively. Because such dramatic changes had been effected in case 1, the same therapy was instituted in this patient on her first visit. Examination on March 19, 1958, revealed external disappearance of the uterine corpus, with its return to its normal position, although a cystocele was present upon straining. The dosage of orally given estrogenic substance was reduced to every other day, principally because of breast soreness. This dosage has been maintained with no return of procidentia, although she has suffered another coronary attack.

Case 3.—A 72-year-old woman was first seen on Nov. 15, 1957. She had never been pregnant. She reported as a patient because of symptoms which were referable to uterine prolapse. Pelvic examination revealed a small cervix, normal in appearance, but on straining it protruded outside of the introitus about a centimeter. The uterine corpus was atrophic but otherwise not abnormal. The adnexal regions were also normal. A cystocele and rectocele were present. Urinalysis revealed the presence of sugar (4+). Her blood pressure was 160/80 mm. Hg. She also had a rather marked skin psoriasis on both the upper and lower extremities. A week later pelvic examination revealed the same findings, and she was referred to an internist for the control of her glycosuria. Her fasting blood sugar level was 128 mg.%. She returned on Feb. 27, 1958, with a prolapse which was complete, the entire uterine corpus and cervix being outside of the introitus. The patient was extremely uncomfortable. She was advised to have this condition corrected by surgical intervention, inasmuch as the present glycosuria had been corrected. She refused surgery and was again seen on April 2, 1958, at which time time she requested some means of therapy other than surgery. She was given the same dosage of orally administered conjugated estrogenic substances and parenterally injected estrone as was used in case 1 and 2.

She was seen 10 days later. The procidentia had disappeared, and the patient stated that after a week's therapy "she felt the uterus snap back into its normal position." Her initial dosage of estrogen has been maintained with no untoward results.

Case 4.—A 65-year-old woman had borne three children, with normal deliveries and postpartum courses. She now complained of a "dropping down sensation of her pelvic organs." Pelvic examination showed marked external hemorrhoids, cystocele, mild rectocele, and a uterine prolapse which brought a small normal-appearing cervix into view 2 cm. outside of the introitus. The uterine corpus was atrophic; the adnexal regions seemed normal. The patient's blood pressure was 136/74 mm. Hg, and the urinalysis was negative. She had previously been seen in 1956, because she had been told she had a "uterine tumor," and pelvic examination at that time had revealed a small fibroid at the fundus in an otherwise normal uterus. There was no evidence of prolapse, but a urethral caruncle and a mild cystocele were noted, although the latter had previously been repaired surgically.

Slides prepared with Papanicolaou's stain showed a low estrogenic level, with no keratinization of cells and no tumor cells. The patient was averse to any further surgical correction. She was put on a trial of conservative estrogenic therapy, as described in cases 1, 2, and 3. After one week's therapy, she stated that she felt "everything tightening up in the region of the pelvic organs," and she further stated that the procidentia no longer existed. Pelvic examination on May 5, 1958, showed the uterine corpus to be normally placed, although a cystocele still persisted.

Comment

No conclusions are being drawn from the findings in the four patients with uterine prolapse who received conjugated estrogens orally and parenterally, since they represent such a small clinical study. However, it is a striking clinical finding that in all four cases the uterine procidentia seems to have disappeared after the administration of estrogenic hormones. This may be just an accidental finding in the patients studied, as a similar happening cannot be found described in the literature.

If one were to conjecture as to the physiological reason for the correction of the uterine herniation, one would naturally surmise that some action had taken place within the supporting structures of the uterus, namely, the cardinal ligaments, thereby causing the uterus to be "pulled up" into its normal habitat. No unanimity of thought regarding the action of the estrogens upon uterine supporting tissue is expressed by endocrinologists, although Hamblen [3] states that lack of estrogens causes the ligaments of the uterus to involute, thereby losing much of their muscular constitution and strength, and they become thin fibrous bands and, hence, poor supporting tissue. It might be logical to expect that the restoration of normal estrogen levels might restore tone and strength to these vital uterine supports.

It is highly desirable that a much larger series be studied under similar clinical conditions and, in addition, an exhaustive physiological laboratory endeavor be assumed in order that the action of estrogens on uterine supporting tissues be determined.

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TROCHANTERIC SYNDROME

CALCAREOUS AND NONCALCAREOUS TENDONITIS AND BURSITIS ABOUT THE TROCHANTER MAJOR

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The trochanteric syndrome frequently masquerades as sciatica. Tenderness and pain in the region of the trochanter major, often with irradiation of this pain down the posterolateral aspect of the thigh, constitute a well-defined syndrome. This symptom pattern is analogous to the so-called bursitis of the shoulder. The locus of pathology is in the abductor mechanism of the hip. The cause of the primary form is wear and tear, that of the secondary form the presence of foreign material, such as the end of a hip nail. Roentgenograms often reveal calcification in the tendons inserting into the trochanter. The condition is not rare. Local injection of hydrocortisone relieves the symptoms of the primary type.

Tendonitis, tenosynovitis, and bursitis about the glenohumeral joint are well known to the profession. These conditions are recognized and lumped together by the laity as bursitis of the shoulder. The analogous conditions in the region of the trochanter major are not so common or well known. However, they are not rare and are of importance in the differential diagnosis of hip and low back pain with and without irradiation.

The anatomic structures morbidly involved in the trochanteric syndrome can include the tendons of the gluteus maximus, gluteus medius, and gluteus minimus and the bursae separating those tendons from trochanter major. The principal bursa measures 2 to 4 by 4 to 6 cm. and lies between the gluteus maximus, as it passes to insert into the iliotibial band, and the trochanter major.[1]

As in the shoulder, one of the factors in the etiology of the primary trochanteric syndrome is the microtrauma of everyday use. Goldenberg and Leventhal [2] found an incidence of trochanteric calcification in 5.4% of 550 hip roentgenograms in patients over the age of 15 years. In the series reported by Spear and Lipscomb [1] the average age in patients with trochanteric bursitis without calcification was 39 years and the average age in those with calcification in the insertion of the gluteus medius tendon 49. In those persons with calcification in the tendon of the gluteus minimus the average age was 45. In the present group of 18 cases of primary trochanteric syndrome the average age was 46 years. Isolated trauma occurred immediately prior to the onset of symptoms in 22% of the cases. In Goldenberg and Leventhal's series of 25 cases with calcification there was a history of injury in 64%.[2] As in the analogous condition of the shoulder, it is felt that the principal factor in etiology is wear and tear rather than a single insult. The remembered injury makes the condition symptomatic. Trochanteric bursitis occurs secondary to operative intervention.

From the El Paso Orthopaedic Surgery Group.

Pathology

The trochanteric syndrome arises from a varying pathology. Spear and Lipscomb [1] reported the syndrome in 67 cases. In 24 of these there was a calcareous deposit near the trochanter. The present series showed calcification in 28%. Goldenberg and Leventhal [2] believe that the calcification occurs in the tendon of the gluteus medius, in a bursa between the tendon of the gluteus medius and the greater trochanter, and under the gluteus medius not connected with the trochanter. Actually, the common sites of calcification are in the tendon of the gluteus medius and minimus. Calcification in the tendon of the gluteus medius is seen at the upper half or third of the lateral facet of the trochanter major. This calcification varies in size from a fleck to an area of several centimeters (fig. 1). Calcification in the gluteus minimus is at the tip of the greater trochanter and usually is smaller than 1 cm. in diameter (fig. 2).

Fig. 1.—Calcium at lateral facet of trochanter major, indicating calcific tendonitis in gluteus medius.

The microscopic pathology in a calcific deposit is similar to that of calcareous tendonitis of the shoulder.[3] In the absence of calcification, there is a serous inflammation of the bursa between the trochanter and the gluteus maximus.

Trochanteric bursitis and calcareous tendonitis are not common; on the other hand they are not rare. Cloyd reported 80 cases of bursitis of the

Fig. 2.—Calcareous deposit in gluteus minimus at its insertion into trochanter major.

shoulder and 10 of the hip.[4] Spear and Lipscomb,[1] of the Mayo Clinic, reported 43 cases of bursitis and 24 cases of calcification seen in the period of 1935 to 1948. Goldenberg and Leventhal [2] reported calcification in 5.4% of 550 consecutive x-rays of the hip made of persons older than 15 years of age. The present series of 18 cases, diagnosed in the years 1955-1957, represent approximately 0.1% of patients seen in a private orthopedic practice. The literature to 1941 is reviewed by Schein.[5] Subsequent series of cases are presented by Spear and Lipscomb [1] and by Cloyd.[4]

Clinical Picture

The clinical picture of the trochanteric syndrome varies in degree but is fairly uniform as to type. The onset is frequently sudden, with pain on the lateral aspect of the hip irradiating down the the posterolateral aspect of the thigh. This irradiation can simulate referred pain from the lumbosacral area. A gluteal limp is frequently present. Local tenderness in the region of the trochanter major is constant except in some isolated cases of calcification in the gluteus minimus tendon where the pathology is deep.[1] When the bursa underlying the gluteus maximus is involved, the hollow over the trochanter is sometimes obliterated. The site of the trochanter can be identified, even in obese persons, by this hollow (fig. 3). Those motions which relax the abductors of the hip tend to diminish the pain, whereas those which tighten these muscles increase it. Thus, passive internal rotation and abduction are painful, and passive abduction and external rotation are not. Flexion and extension of the hip do not cause severe pain. The most constant and useful finding is local tenderness over the trochanter major. In the presence of an active calcareous deposit, as in the case of calcareous tendonitis of the shoulder, a low-grade fever and leukocytosis may be present.

Roentgenographic study demonstrates the absence of intra-articular pathology except when this is an incidental finding. Some of the patients of this age group will show hypertrophic changes. Roentgenographic examination may show a primary condition, such as a hip nail causing a secondary bursitis. Calcifications of the tendons of the gluteus medius or minimus may be seen (fig. 1 and 2).

The treatment of the primary trochanteric syndrome follows that used for its analogue in the shoulder. Roentgenotherapy, diathermy, puncture, and open surgical removal of calcium when this is present have been used with good results.[6] In this series of 18 cases, local injection of hydrocortisone acetate has resulted in complete relief of symptoms in all instances. The technique employed is that of infiltration of all tender areas with a local anesthetic

Fig. 3.—Hollow on lateral aspect of hip, indicating tip of trochanter major.

followed by infiltration of these areas by hydrocortisone in doses of 25 to 100 mg. The patient should be cautioned that the pain may be temporarily aggravated and that more than one injection may be necessary. Trochanteric bursitis secondary to the presence of extraneous material should be treated by removal of the foreign substances.

Summary

"Bursitis" of the shoulder has its analogue about the hip. It is not uncommon and can result in a train of clinical signs and symptoms identified as the trochanteric syndrome. This syndrome is sometimes confused with referred pain from the lumbosacral area. It is effectively treated by local injections of hydrocortisone.

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SIMPLE SURGICAL TREATMENT OF SPONTANEOUS PNEUMOTHORAX BY USE OF A PLASTIC NEEDLE

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and
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When the physician encounters a patient with spontaneous pneumothorax, several courses of therapy are available. For purposes of simplification it may be stated that the two general methods are the medical or "watchful expectancy" program and the surgical or aspiration method. Whereas 30 years ago treatment was principally limited to medical management, it has become increasingly more common to utilize the aspiration method. There are several reasons for this change, which are as follows: (1) earlier reexpansion of lung, (2) immediate relief of symptoms, (3) lower incidence of complications, (4) shorter period of hospitalization, and (5) an earlier return to economic productivity. It has been customary to refer to the medical or nonaspiration program as the conservative program. We are in agreement with the principles expressed in the paper by Campbell and Varco [1] in which they state that the medical management is "scarcely conservative of the patient's comfort, convenience, finances or predisposition to serious complication."

In spite of the evidence favoring early surgical management, an appreciable number of patients with spontaneous pneumothorax are not treated by early aspiration. The reasons for this are varied, but it is believed that if the procedure could be made both simple and completely safe this method would be universally adopted. The device to be described is believed to fulfill these requirements.

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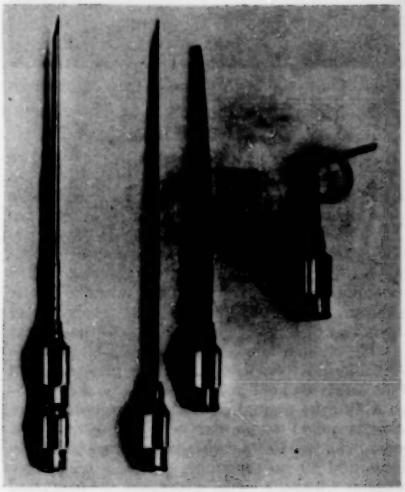

Fig. 1.—Plastic needle, assembled unit on left and component parts in middle. Note degree of torsion permissible without significant luminal obstruction.

The patient usually presents himself with the complaint of chest pain, dyspnea, or cough. Occasionally there may be no complaints whatever and

the diagnosis is established on the basis of routine physical examination or survey chest x-ray. If the degree of collapse is 15% or less, surgical management is not indicated. When a greater degree of pneumothorax exists, the following method of treatment is employed.

Fig. 2.—Chest roentgenogram of healthy young adult with spontaneous pneumothorax.

Method

The plastic needle to be used is shown in figure 1. The needle is shown in its assembled state on the left and disassembled in the middle; the needle on the right shows the degree of torsion which can occur without significant obstruction of the lumen. The patient is placed in the dorsal recumbent position and the anterolateral part of the chest wall is cleansed with thimersol (Merthiolate) or a similar bacteriocidal agent. The general principles of asepsis are observed. The second interspace near the midclavicular line is infiltrated with 1% procaine hydrochloride (Novocain), and the plastic needle which has been kept in a sterile pack is then introduced into the pleural cavity. A characteristic sensation is noted when the needle punctures the pleura. The needle is then advanced several millimeters, and the metallic inner portion is withdrawn the same distance. This procedure is continued until the entire plastic portion is within the pleural cavity and the metallic portion has been completely removed. Aspiration of air is then begun either with use of a 50-cc. syringe attached to a three-way stopcock or by attachment of the needle to an air pump set at minus 10 cm. of water. The air is withdrawn slowly to prevent paroxysms of coughing due to tracheal and mediastinal shift and reexpansion of lung parenchyma. In the event of persistent coughing, 1/6th grain (10 mg.) of morphine sulfate should be administered intravenously to depress the cough reflex. On complete reexpansion of the lung, the base of the needle is taped to the chest wall, and negative pressure is maintained for 24 hours after all air leakage has ceased. Some authors have recommended the use of water seal drainage. Undoubtedly the results with its use are completely satisfactory. It has been our practice to use negative pressure systems with pumps, and the results thus far have been excellent. The use of an air pump does not encourage a persistent pleural air leak, contrary to the opinion expressed by some. Figures 2 and 3 show the typical pretreatment and post-treatment chest roentgenograms which are seen after treatment in the manner described.

Since the original work with the use of the plastic needle in treatment of pneumothorax, we have been impressed with its usefulness in diagnostic and therapeutic puncture of other serous cavities. Thus, pericardiocentesis and abdominal pericentesis can be performed with a further degree of safety. In addition, for those who treat hydrocele by aspiration, traumatic orchitis can be avoided by use of this device.

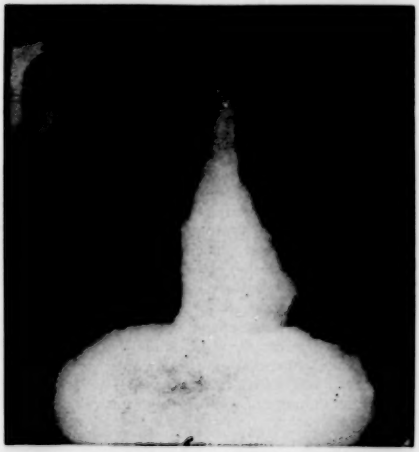

Fig. 3.—Chest roentgenogram showing reduction of pneumothorax and position of plastic needle.

James H. Rose Jr., Mrs. Martha Hassell, and Velma L. Hofferbert supplied technical assistance in this study. T. E. Gauthier, Rochester Products Company, Rochester, Minn., supplied information on the plastic needle and furnished figure 1.

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PRESERVATION OF RENAL FUNCTION DURING PARTIAL NEPHRECTOMY

USE OF RUBBER BAND TOURNIQUET FOR HEMOSTASIS

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Murphy and Best,[1] in 1957, reviewed the literature concerning partial nephrectomy. In their concise and useful paper they recommended simple guillotine amputation and presented convincing evidence that the least damage is done to the kidney with this technique. They described hemostasis as secured during the resection by placement of a Crafoord clamp on the vascular pedicle. One of us (W. E. G.) has previously reported use of a small bulldog clamp placed on the renal artery alone during biopsy or partial nephrectomy.[2] Recently, we have had occasion to use a different technique for hemostasis during partial resection and have found it simple and effective.

The kidney is well mobilized, allowing access to all of its surfaces. The area to be resected is identified, and the renal capsule is stripped from the area which is to be removed. At a point on the normal kidney, below the area of stripping, a rubber band, ¼ in. wide, is placed around the whole kidney as a tourniquet and is held in place with a clamp. This allows perfect hemostasis and good access to the area to be resected. The amputation is then done as described by Murphy and Best [1] (see figure). Hemostatic sutures are placed under direct vision. The capsule is closed over the wound. The rubber band tourniquet is released, and the wound is carefully inspected for evidence of any excess bleeding.

This simple technique is useful in resection or nephrotomy of either pole of the kidney. It is not applicable to resection or biopsy of the central portion of the kidney, in which case we feel that the use of a bulldog clamp placed on the isolated renal artery is the method of choice. Although we have not yet used this type of tourniquet for hemostasis in dividing the isthmus of a horseshoe kidney, it would seem ideally suited to this situation with the application of two tourniquets and incision in the isthmus of the horseshoe kidney between them.

The use of a tourniquet in this manner to achieve renal hemostasis has the added advantage of allowing continued circulation to the remaining normal kidney tissue. It could also be applied in the rare situation when partial resection of a solitary kidney is necessary for renal neoplasm.[3]

From the Department of Surgery, Division of Urology, University of California Medical Center, and Wadsworth General Hospital, Veterans Administration Center.

We have employed this technique in two cases with excellent results, and some of our associates have also used it with satisfaction after learning of the method from us. On two occasions a colleague had difficulty with complete hemostasis because the rubber band was too thin and was not pulled tightly enough. The rubber band tourniquet should be a heavy, ¼-in., strong band, and it should

Rubber band tourniquet, used to achieve local hemostasis without impairment of blood supply to rest of kidney during partial nephrectomy.

be applied tightly enough to produce blanching of the kidney. When properly used, it provides a bloodless field and minimal trauma and is easy and practical in application.

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SLIDE LATEX FIXATION TEST

A SIMPLE SCREENING METHOD FOR THE DIAGNOSIS OF RHEUMATOID ARTHRITIS

Jacques M. Singer, M.D.
and
Charles M. Plotz, M.D., New York

The use of uniform size polystyrene latex particles as substitutes for red blood cells in the serologic test for rheumatoid arthritis has been reported on previously.[1] These biologically inert particles might agglutinate spontaneously without added gamma globulin in the presence of strongly positive rheumatoid serum, but only in a low titer.[2] When serums were fractionated by the addition of 1.64 M ammonium sulfate, 90% of 250 patients with rheumatoid arthritis showed positive results in a one-tube technique with use of the patient's own gamma globulin.[2a] As a further simplification, Bozicevich and co-workers [3] have described a slide method using serum and bentonite particles. A study has now been made which has resulted in a simple screening test which is highly sensitive for the diagnosis of rheumatoid arthritis and suitable for epidemiologic study, as well as for clinical and office use.

Materials and Methods

A stock solution of a suspension of polystyrene latex particles of uniform size, 0.81 μ in diameter, is made by diluting the original suspension with distilled water. Dilution is continued until 0.1 ml., when mixed with 10 ml. of water, matches a light transmission of 5% in a Coleman Universal spectrophotometer (model 11 or 14) in a square cuvette, 13 by 13 by 100 mm., at 650 mμ with a red filter. This stock solution may be stored in the refrigerator for several months.

One per cent and 2% solutions of eosin are prepared with distilled water. Three pipets, with a serologic capacity of 0.2 ml. with 0.01-ml. subdivisions, or dropping bottles with glass pipets calibrated to deliver 0.05 ml. of liquid in one drop, are used, one containing the stock latex particles and one each for the 1% and 2% eosin solutions. Wooden toothpicks and ordinary microscope slides are also needed.

First, 0.2 ml. (three to four drops) of fingertip blood (or 0.05 ml. of serum) are placed on each of two slides. One drop (0.05 ml.) of 1% eosin is added to the blood on one slide and one drop of 2% eosin to the other. Both are then mixed thoroughly with a toothpick. Two drops (0.01 ml.) of stock latex solution are added to each slide, they are again mixed, and the resulting suspension is spread over the slides by tilting them back and forth.

With use of natural or artificial daylight and a dark background, the slides are then tilted back and forth with the fingers and observed for clumping. In positive tests, this will appear in one to three minutes as a fine granular agglutination. Negative tests show a simple homogeneous reddish suspension. No magnification is required.

The order of addition should be carefully followed—blood, eosin, then latex—since, if latex is added before the eosin, nonspecific agglutination may occur. The concentration of eosin is critical. If the concentration of eosin is well below 1%, a much greater incidence of false agglutination is observed, and, if eosin is eliminated altogether, 85% of all serums will show nonspecific agglutination. A positive test is one in which agglutination occurs on either slide.

Comparison of Positive Results with Tube and Eosin Slide Latex Fixation Tests in 738 Patients*

	Latex Fixation Test					
			Eosin Slide Method			
	Tube Method*		1%		2%	
Clinical Group, No. of Patients	No.	%	No.	%	No.	%
Rheumatoid arthritis, 120	108	90.0	110	91.6	104	86.6
Osteoarthritis and other arthritis, 180	5	2.7	8	4.4	5	2.7
Lupus erythematosus, 38	5	13.1	6	15.7	4	10.5
Other nonarthritic disease, 300	9	3.0	26	8.6	8	2.6
Normal, 100	2	2.0	2	2.0	1	1.0

* With use of patient's own gamma globulin.

Results

A total of 120 patients with rheumatoid arthritis, 38 patients with disseminated lupus erythematosus, 180 patients with osteoarthritis and other forms of arthritis, 300 patients with nonarthritic diseases, and 100 normal controls were tested. The results are summarized in the table. This table compares the results observed with the one-tube latex fixation test with use of the patient's own gamma globulin and the results with the 1% and 2% eosin slide test. There is close correlation in all groups. As may be observed from the table, with use of 2% eosin, the incidence of positive slide tests in patients with rheumatoid arthritis is reduced from 91.6%, observed with 1% eosin, to 86.6%. In nonarthritic disease, however, the incidence of positive results is reduced from 8.6%, tested with 1% eosin,

From the Arthritis Clinic and the departments of medicine and microbiology, Mount Sinai Hospital. Fellow of the Arthritis and Rheumatism Foundation (Dr. Singer), and Director of Arthritis Clinics, Mount Sinai and Kings County hospitals (Dr. Plotz).

to 2.6% when tested with 2% eosin. If the increased sensitivity is important, as in epidemiologic study, the slide test with 1% eosin might be more useful. On the other hand, the 2% eosin test gives fewer positive reactions in cases of nonrheumatoid arthritis.

Summary

A new simplified screening slide agglutination test for the serologic diagnosis of rheumatoid arthritis consists of the addition to fingertip blood or serum of an eosin solution and latex particles. The resultant agglutination in positive tests is read easily and quickly with the naked eyes. While 86.6% of 120 patients with rheumatoid arthritis gave positive results with the 2% eosin slide agglutination method, only 2.7% of serums of 180 patients with other arthritic disease, 2.6% of 300 patients with nonarthritic diseases, and 1% of 100 normal controls were found to show positive findings.

860 Fifth Ave. (Dr. Plotz).

The polystyrene latex particles used in this study were manufactured by the Dow Chemical Company, Midland, Mich., and distributed by the Arthritis and Rheumatism Foundation, New York.

This study was aided, in part, by grants from the National Institute of Arthritis and Metabolic Disease, National Institutes of Health, the State of New York chapter of the Arthritis and Rheumatism Foundation, and the Fribourg Fund.

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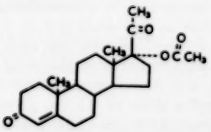
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations.

H. D. KAUTZ, M.D., *Secretary.*

Hydroxyprogesterone Acetate.—17α-Hydroxyprogesterone acetate.—The structural formula of hydroxyprogesterone acetate may be represented as follows:



Actions and Uses.—Hydroxyprogesterone acetate is an esterified derivative of hydroxyprogesterone. In contrast to progesterone, which is virtually inactive by the oral route, hydroxyprogesterone acetate causes pronounced progestational effects after oral administration. Typical effects include production of secretory changes in an estrogen-primed endometrium, luteal changes in exfoliated vaginal epithelial cells, suppression of the formation of fern-like patterns in the cervical mucus (arborization), increases in basal body temperature, and induction of endometrial withdrawal bleeding after endogenous or exogenous estrogenic stimulation. On the basis of both laboratory and clinical studies, hydroxyprogesterone acetate appears to be considerably more potent as a progestogen than are equal amounts of orally given ethisterone. Its onset and duration of action are approximately the same as with parenterally administered progesterone; withdrawal bleeding from an estrogen-primed endometrium generally occurs within two to three days after the oral administration of about 100 mg. The drug produces only minimal estrogenic responses and shows no androgenic activity.

Hydroxyprogesterone acetate is useful in all conditions in which parenterally administered progesterone or hydroxyprogesterone caproate is indicated. (See the monograph on hydroxyprogesterone caproate in New and Nonofficial Drugs.) Thus, it may be given for the treatment of primary or secondary amenorrhea, for functional uterine bleeding in pa-

tients with diagnosed benign endometrial hyperplasia, and in cases of infertility believed to be due to inadequate corpus luteum function. The drug may also be employed during the first and second trimesters in patients with a history of habitual abortion. There is inadequate evidence at hand to justify the routine employment of hydroxyprogesterone acetate, or any other progestogen, for the treatment of dysmenorrhea or premenstrual tension.

Hydroxyprogesterone acetate appears to be well tolerated. In the clinical studies to date, no significant untoward effects have been reported.

Dosage.—Hydroxyprogesterone acetate is administered orally. For amenorrhea, functional uterine bleeding, and infertility, the usual dosage ranges from 25 to 50 mg. per day. This amount is taken either for 5 successive days beginning on the 21st day of the menstrual cycle or for 20 successive days beginning on the 5th day of the menstrual cycle. Supplemental estrogen therapy may also be instituted in patients who fail to produce adequate amounts of endogenous estrogen. The proposed dosage for habitual abortion is 200 to 400 mg. daily until fetal viability is evident.

Preparations: tablets 25 mg. and 50 mg.

Applicable commercial name: Prodox.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of hydroxyprogesterone acetate.

Influenza Virus Vaccine, Monovalent, Type A (Asian Strain).—A sterile suspension of formaldehyde-killed influenza virus, type A, Asian strain, recovered from the extraembryonic fluids of chick embryos infected with this virus. The product complies with the requirements of the National Institutes of Health of the United States Public Health Service. Influenza virus vaccine, Asian strain, monovalent, has been standardized to date in terms of chicken-cell agglutination (CCA) titer. Most lots of vaccine released by the NIH prior to Dec. 1, 1957, contained 200 CCA units per cubic centimeter, but all lots after that date will contain 400 CCA units per cubic centimeter.

Actions and Uses.—Influenza virus vaccine, monovalent, is designed solely for prophylaxis against epidemic and endemic infections caused by the type A, Asian strain, of influenza virus. A rise in hemagglutination-inhibition antibody titers against Asian strain influenza virus has been demonstrated after injection of the vaccine into both man and animals. In man, the rise is apparent within one week after subcutaneous injection, and maximal antibody titers appear to be achieved by the end of the second week. Some recent evidence indicates that the more potent vaccine containing 400 CCA units may elicit antibody responses comparable to those observed in patients who have recovered from Asian influenza. Hemagglutination-inhibition antibody titers produced by vaccines containing other strains of influenza virus have been found to be correlated with the development of immunity against the disease caused by those strains. As yet, clinical experience with the new Asian strain is not sufficient to permit such a correlation. In a single small series of patients, unvaccinated and vaccinated adult volunteers were inoculated with live Asian strain influenza virus; 78% of the unvaccinated placebo group became ill with influenza, whereas 44% of the vaccinated group developed symptoms of this disease. These preliminary results give some indication that the vaccine provides moderate, but incomplete, protection against Asian influenza. At the present time, therefore, it can only be assumed that the present vaccine may be similar to other influenza virus vaccines which have given variable protection, up to 70% in some instances. The period of protection provided by the new vaccine is unknown but, on the basis of experience with other influenza vaccines, can be expected to last for about one year. No significant effect on Asian influenza antibody response, either adverse or beneficial, has been demonstrated when the Asian strain component is administered in combination with the old polyvalent A,A′, and B vaccine.

Since the virus for the vaccine is grown in the extraembryonic fluid of chicken eggs, administration of vaccine is absolutely contraindicated in persons with a history of hypersensitivity to egg, chicken, or chicken feathers. Local reactions to the vaccine are common and include a transient stinging sensation at the site of injection immediately after administration, usually with local redness, induration, and tenderness during the succeeding 12 to 24 hours. A systemic type of reaction characterized by fever, malaise, backache, and headache occurs in an appreciable proportion of patients to whom the vaccine is given subcutaneously; the incidence is considerably lower if the vaccine is administered intracutaneously. Such systemic reactions are usually not serious and rarely incapacitate the patient for longer than one day.

Dosage.—Influenza virus vaccine, monovalent, type A (Asian strain) is administered subcutaneously. The dose by this route is 1 cc. for adults and 0.5 cc. for children between the ages of 5 and 12 years. For children between the ages of 3 months and 5 years, the American Academy of Pediatrics has suggested a dose of 0.1 cc. given subcutaneously or intracutaneously. The academy has also suggested that the foregoing doses for infants or children be repeated within one or two weeks.

Vaccination of adults by two intracutaneous injections of 0.1 cc. separated by an interval of three to four weeks has been suggested. There is some evidence to indicate that the antibody response after the intracutaneous injection of 0.1 cc. is appreciable, but not as good as that which follows subcutaneous injection of 1 cc. Such a regimen

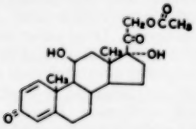
reduces the amount of vaccine needed and, no doubt, is attended by a reduced incidence of systemic reactions. However, it is difficult to predict its clinical efficacy since, in the past, all other field evaluations of influenza vaccines have been carried out with the drug administered by the subcutaneous route.

Preparations: suspension (injection) 5 cc. and 10 cc.

Applicable commercial name: Influenza Virus Vaccine, Monovalent, Type A (Asian Strain).

Eli Lilly and Company; The National Drug Company; and Pitman-Moore Company, Division of Allied Laboratories, Inc., cooperated by furnishing scientific data to aid in the evaluation of influenza virus vaccine, monovalent, type A (Asian strain).

Prednisolone Acetate.—Prednisolone-21-acetate.—The structural formula of prednisolone acetate may be represented as follows:



Actions and Uses.—Prednisolone acetate has the same actions, uses, and limitations as prednisolone. The acetate ester is relatively nonirritating to the tissues and is therefore suitable for intramuscular injection. It may be used in those situations in which oral therapy with prednisolone is not feasible. The drug is also a suitable substitute for orally administered prednisolone in patients undergoing surgery who require maintenance glucocorticoid therapy. (See the monograph on prednisolone in New and Nonofficial Drugs.)

Dosage.—Prednisolone acetate is administered by the intramuscular route. Dosage is expressed in terms of the parent drug and is the same as for orally administered prednisolone.

Preparations: suspension (injection, aqueous) 125 mg. in 5 cc.

Applicable commercial name: Sterane.

Pfizer Laboratories, Division of Chas. Pfizer & Company, Inc., cooperated by furnishing scientific data to aid in the evaluation of prednisolone acetate.

Use of Poliomyelitis Immune Globulin (Human) for Oral Herpetiform Lesions

The Council has evaluated the use of poliomyelitis immune globulin (human) for the management of recurrent vesicular lesions of the mouth. Because this preparation of gamma globulin has been useful for the attenuation or prevention of such virus diseases as poliomyelitis, measles, and infectious hepatitis, it has been tried also for the treatment of certain oral lesions believed to be viral in origin. These lesions are collectively designated as oral herpetiform lesions, since the etiology of all types has not been proved to be herpes simplex. This designation includes herpetic gingivostomatitis, herpetic ulcers, herpes labialis (cold sore, fever blister), and aphthous stomatitis (canker sore, aphthous ulcer).

The clinical evaluation of poliomyelitis immune globulin (human) used for this purpose is based upon a few individual case reports taken from a relatively small number of patients to whom the drug was administered for short periods of time. In some cases, therapy was begun after the original lesions had undergone considerable secondary infection, thus complicating the diagnosis and interpretation of results of therapy. Although controlled data are lacking, some physicians and dentists believe that some, but not all, patients are benefited by such therapy; other investigators have been unable to demonstrate beneficial effects. The drug does not appear to have any appreciable effect on lesions already present. In favorable cases, it seems to halt the formation of new lesions. The duration of immunity thus produced is unknown. The results obtained thus far warrant further study under well-controlled conditions. At the present time, however, the use of poliomyelitis immune globulin (human) for the treatment of oral herpetiform lesions is considered experimental.

In the clinical trials to date, dosage appears to be determined on an empirical basis. Equally satisfactory results have been reported with doses ranging from 2.5 cc. every three or four days to as much as 20 cc. every day for six weeks in cases of Behcet's syndrome. As a general rule, it is suggested that 3 to 10 cc. be injected intramuscularly once or twice a week. Subsequent dosage and intervals between injections should be governed by individual response. Further studies are needed, however, to establish both the effect of poliomyelitis immune globulin (human) and its optimal dosage.

The Council voted to expand New and Nonofficial Drugs to describe the use of poliomyelitis immune globulin (human) for oral herpetiform lesions.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of this additional use of poliomyelitis immune globulin (human).

Ristocetin.—An antibiotic produced by the fermentation of Nocardia lurida, a species of Actinomycetes. The antibiotic has two components, ristocetin A and ristocetin B, the chemistry of which is not completely known. The commercial product is a lyophilized preparation representing a mixture of ristocetins A and B.

Actions and Uses.—Ristocetin is an antibiotic substance active against pathogenic gram-positive cocci. It is active in vitro against the following

organisms (listed in order of decreasing susceptibility): streptococci, enterococci, pneumococci, and staphylococci. It also shows in vitro activity against mycobacteria, although it is not recommended for use in human tuberculosis infections at the present time, since clinical evidence of its efficacy is lacking.

The principal therapeutic tests of the efficacy of ristocetin have been in the treatment of severe staphylococcic and enterococcic infections. Since the drug is not as active, as a rule, as penicillin and certain other antibiotics, and since it must be given intravenously, it is neither rational nor practical to employ ristocetin for treating staphylococcic infections unless certain criteria have been met. Accurate bacteriological identification of staphylococci should be made prior to initiating therapy. Sensitivity tests should be done to establish not only the sensitivity of the bacteria to ristocetin but also their resistance to such other agents as penicillin, the tetracyclines, streptomycin, erythromycin, chloramphenicol, and perhaps novobiocin and oleandomycin. In some patients treated for severe staphylococcic infections, ristocetin has been successful in arresting infections due to strains of the organism that have resisted therapy with all other available agents. Thus, the drug shows promise as a valuable antistaphylococcic agent which may be lifesaving in cases in which organismal resistance precludes the use of other antibiotics.

Ristocetin is also of value for the treatment of enterococcic infections, particularly endocarditis caused by that organism. In view of the marked sensitivity of enterococci to the drug and the frequency with which these organisms are resistant to other antibiotics, ristocetin may ultimately prove to be a drug of choice for the initial therapy of serious infections due to enterococci resistant to other antimicrobial agents.

Because ristocetin inhibits, in vitro, the growth of pneumococci and beta-hemolytic streptococci (group A), it has been proposed for use in infections caused by these organisms. Limited experience with such infections indicates that the drug is capable of effecting a cure. Since, however, other antibiotic agents (chiefly penicillin and the tetracyclines) are generally better tolerated, are easier to administer, and are effective, and since bacterial resistance to the other agents rarely, if ever, develops, there is practically no justification for the use of ristocetin in pneumococcic or beta-hemolytic streptococcic (group A) infections.

To date, bacterial (principally staphylococcic) resistance to ristocetin apparently has not developed in vitro or in vivo to the same degree as with certain other antibiotics. It is not yet known whether resistant forms will appear as the clinical use of the drug becomes more extensive. Cross resistance to other antibiotics has not been reported.

Ristocetin produces a number of side-effects, some of which may prove to be serious. Significant depression in white blood cell counts, with relative neutropenia, has been reported in about 4% of cases studied to date. Abnormal bone marrow changes or granulocytopenia have not yet been observed, but physicians should be alert to their possible occurrence. Peripheral blood cell counts, including a differential leukocyte count, should be done at frequent intervals and therapy discontinued immediately if the total white blood cell count falls below 5,000 per cubic millimeter or the differential neutrophil count falls below 50%. In some patients who subsequently develop leukopenia, eosinophilia is observed as an early sign.

Ristocetin is irritating to the intima of veins, and chemical thrombophlebitis can be produced if the drug is administered in too high a concentration. Hence, only diluted solutions are suitable for intravenous infusion, and care should be taken to avoid accidental extravasation after displacement of the infusion needle. Drug fever, sometimes accompanied by a skin eruption, has been observed in a few patients after several days of therapy with ristocetin. This has subsided promptly upon discontinuation of medication. Diarrhea may occur occasionally in patients receiving high doses. The drug can also elicit occasional allergic responses, generally skin rashes either at the site of infusion or, more commonly, a generalized eruption. No anaphylactic reactions have been reported. Although the drug has not been reported to cause toxic effects on the kidneys, periodic urinalyses are considered advisable.

Dosage.—Ristocetin should be administered only by the intravenous route, because it is inadequately absorbed when given orally and because it is irritating to the tissues when given extravascularly. The drug is best administered by the drip technique. For this purpose, dry, sterile powder is dissolved in a sufficient amount of 5% dextrose solution to make a 0.2% solution (2 mg. per cubic centimeter). The required volume of this diluted solution is then administered by the intravenous route over a period of 35 to 45 minutes. Occasionally, more concentrated solutions have been given by direct intravenous injection. The maximum tolerated concentration of such solutions is 1.25% (12.5 mg. per cubic centimeter), and the maximum rate of injection is 2 cc. (25 mg.) per minute.

For staphylococcic infections, the usual total daily dose is 25 to 50 mg. per kilogram of body weight. In endocarditis due to resistant strains of staphylococci, or when vegetations or abscesses are present, dosages as high as 75 mg. per kilogram may be used. This is equivalent to 6 Gm. per day for an adult weighing 75 kg. (165 lb.) and is considered the maximum dosage. For acute or sub-

acute endocarditis due to enterococci, the usual dose is 25 mg. per kilogram of body weight. However, doses as high as 50 mg. per kilogram are occasionally employed, depending on clinical response, tolerance, and severity of the infection.

The foregoing total daily doses are given in two or three divided doses at intervals of 8 or 12 hours. The lower dosages indicated suffice for the majority of infections in which ristocetin may be used. It is emphasized that dosages in excess of 2 to 3 Gm. per day are very rarely required. At this dosage level, side-effects are relatively uncommon. If there is no response within 10 to 12 days, indications for the use of ristocetin should be critically reviewed. Since staphylococcic sepsis tends to recur promptly unless almost all staphylococci are eliminated, treatment should be continued for several days after a definite clinical response has been obtained.

Since ristocetin leaves the body mainly in the urine, a cumulative effect may be produced in the elderly (over age 65) or in younger patients with impaired renal function. In these patients, the recommended dosage should usually be reduced, and approximately half the normal dosage will usually bring about a good clinical response.

Preparations: powder (injection) 500 mg.
Applicable commercial name: Spontin.
Abbott Laboratories cooperated by furnishing scientific data to aid in the evaluation of ristocetin.

CHEMICAL LABORATORY

The Chemical Laboratory has authorized publication of the following statement.

WALTER WOLMAN, PH.D., *Director.*

Monographs of tests and assays for new and nonofficial drugs adopted by the Chemical Laboratory of the American Medical Association represent an expression of opinion as to what might constitute adequate tests and assays to serve as a reference guide to those interested in the identity and quality of a new and nonofficial drug.

Completed monographs are published in the journal *Drug Standards* for those interested in the details of the procedures. Monographs on the following drugs have appeared in the May-June, 1958, issue of that journal. The cooperation of the listed pharmaceutical firms that furnished samples and data is acknowledged.

Chlorquinaldol.....(Geigy Pharmaceuticals)
Hydroxyzine hydrochloride.....(J. B. Roerig & Co.)
Tricyclamol chloride.....(Burroughs-Wellcome & Co., Inc.)
(Eli Lilly & Company)
Zoxazolamine.....(McNeil Laboratories, Inc.)

POISON IVY.—A definite but limited reduction in Rhus sensitivity may be attained by oral or intramuscular administration of Rhus allergens. With oleoresin, maximum hyposensitization is obtained with approximately 2000 to 2500 mg. intramuscularly and 2500 to 3000 mg. orally. With the pure, but less potent, pentadecylcatechol, this state is reached with approximately 2500 to 3000 mg. intramuscularly and 3500 to 4000 mg. orally. Hyposensitization occurs in a definite pattern revealed by quantitative patch tests. The reaction to the highest dilution declines first. Only the terminal portion of the dosage-response curve is notably affected. More than a hundredfold decrease in titer is rare. A given fraction of the original sensitivity may be abolished but no more, regardless of how high the total dose or the initial degree of sensitivity. By repeatedly assaulting the skin with dermatitis-producing patch tests over a period of many months, complete clinical desensitization to leaves can be achieved. The actuality of "hardening" has been proved. Complete desensitization of the highly sensitive subject by oral or intramuscular administration is impossible. A variety of systemic and mucocutaneous side-reactions may develop in the course of hyposensitization, accompanied by characteristic changes in the blood. The severity and frequency of these are proportional to the dosage and the sensitivity. The legitimate objectives of hyposensitization are in order of probability briefer duration, less dissemination, and milder attacks. Hyposensitization is temporary. It begins to wane after a few weeks. The original sensitivity is gradually regained within 6 to 10 months, occasionally longer.—A. M. Kligman, M.D., Ph.D., Hyposensitization Against Rhus Dermatitis, *A. M. A. Archives of Dermatology*, July, 1958.

COUNCIL ON MENTAL HEALTH

The following report on medical use of hypnosis was developed by the Council on Mental Health constituting itself as a committee of the whole under the chairmanship of Dr. M. Ralph Kaufman, Council member. The conclusions arrived at herein have come about as a result of a two-year study of medical use of hypnosis. The necessity for this was brought sharply to the attention of the Council by increasing interest in this area; there were frequent inquiries from physicians and dentists throughout the United States as to the effectiveness of hypnosis in the medical and dental fields and numerous requests from physicians for information about where proper and thorough training could be obtained.

Preliminary investigation by the Council revealed that centers for training, under proper auspices, were sharply lacking. It was also noted that many courses in hypnosis were being offered to physicians and dentists by groups who, in the Council's opinion, were not properly accredited by any professional school or university. Likewise, courses were being offered to physicians and dentists on the basis of a 5-lesson or 10-lesson course in hypnosis, offered solely as correspondence courses. During the past two years, the Council has consulted with many physicians and dentists known as expert practitioners of hypnosis and also with many persons of other professions who have had a deep interest in and intimate connection with hypnosis and with research in hypnosis. The Council has also reviewed a report on medical use of hypnosis published in the British Medical Journal, *April 23, 1955. It has reviewed information and opinions as noted in the attached bibliography. The publication of the bibliography indicates only that the material therein has been reviewed; it does not mean that opinions and information are necessarily considered authoritative by the Council.*

In substance, the Council's report indicates that there are definite and proper uses of hypnosis in medical and dental practice in the hands of those who are properly trained. It indicates, also, that there is a severe lack of the necessary training facilities, under proper auspices, in the United States and that such centers should be established. The report thoroughly condemns the use of hypnosis for entertainment purposes, because of the adverse effects it can bring when used by persons not thoroughly medically or psychiatrically oriented. This report was approved by the Board of Trustees and the House of Delegates of the American Medical Association at its June, 1958, meeting in San Francisco.

RICHARD J. PLUNKETT, M.D., *Secretary.*

MEDICAL USE OF HYPNOSIS

The history of hypnosis since the time of Mesmer has been characterized by a series of curious cycles alternating between great interest and almost complete rejection. This phenomenon in itself is an indication of the somewhat mystical aura that has surrounded the subject throughout the years. Recently, owing to a concatenation of circumstances, there has been a reawakened interest in hypnosis. In part, the experiences of World War II contributed to this interest.

The Council on Mental Health of the American Medical Association has for some years received numerous inquiries from physicians throughout the United States relating to the subject of hypnosis, many of them asking for information regarding training programs in this area. A group of serious workers in medicine has been reporting on various aspects of the utilization of hypnosis. In addition, the dental profession has become interested in its use in relation to its own practice. Concurrently, "fringe" groups have been exploiting hypnosis through the press, radio, and television. Overpopularization in this as in other areas of medicine usually leads to oversimplification. Overdramatized events are seized on to the general detriment of sober scientific work.

A subcommittee of the British Medical Association has issued an excellent report, which appeared in the *British Medical Journal*, April 23, 1955, and with which the Council is in essential agreement.

In view of the total situation, the Council on Mental Health constituted itself as a committee of the whole to study the medical use of hypnosis. Some outstanding authorities in this field were invited to participate in several committee meetings, and in addition others were requested to give their opinions through correspondence. The Council expresses its thanks and appreciation to them for their excellent collaboration in this study. It is to be emphasized that the responsibility for this report and the recommendations contained therein are those of the Council.

The work of the Hypnosis Committee was limited to the specific theme of the medical use of hypnosis in its therapeutic aspects, since this seemed to be the most relevant area for the Council's consideration.

There was unanimous agreement that there was no need at this time to question the validity of the various phenomena elicited by hypnotic techniques. Actually, in the literature of hypnosis practically all of these phenomena have been noted in one way or another since the time of Mesmer. In spite of this, however, it is still difficult to arrive at a formulation of hypnosis that is completely satisfactory. The subcommittee of the British Medical Association presented the following definition, with which there was agreement in general:

> [Hypnosis is] a temporary condition of altered attention in the subject which may be induced by another person and in which a variety of phenomena may appear spontaneously or in response to verbal or other stimuli. These phenomena include alterations in consciousness and memory, increased susceptibility to suggestion, and the production in the subject of responses and ideas unfamiliar to him in his usual state of mind. Further, phenomena such as anesthesia, paralysis, and the rigidity of muscles, and vaso-motor changes can be produced and removed in the hypnotic state.

The Committee emphasized certain regressive aspects of hypnosis. It also stressed the fact that hypnotic phenomena were of a wide variety and should not be limited only to the so-called trance state.

In order to begin to understand these phenomena it is necessary to place hypnosis within the general framework of psychodynamic psychology and psychiatry. This has implications not only for the theoretical understanding of hypnosis but also for its therapeutic application and will, therefore, be related in an important way to any teaching and training program. In a sense it is unfortunate that the induction of hypnosis is generally so simple a matter that it requires little or no technical skill or training. This, in itself, represents one of the main hazards in its utilization, since it lends itself to oversimplification and overdramatization with a production of spectacular phenomena that are meat for the charlatan. The use of hypnosis has a recognized place in the medical armamentarium and is a useful technique in the treatment of certain illnesses when employed by qualified medical and dental personnel.

It has already been emphasized in this report that a background of psychodynamic psychology and psychiatry is essential in order to understand the phenomena of hypnosis. It is equally important to insist on the fact that the utilization of hypnotic techniques for therapeutic purposes should be restricted to those individuals who are qualified by background and training to fulfill all the necessary criteria that are required for a complete diagnosis of the illness which is to be treated. Hypnosis should be used on a highly selective basis by such individuals and should never become a single technique used under all circumstances by a therapist. No physician or dentist should utilize hypnosis for purposes that are not related to his particular specialty and that are beyond the range of his ordinary competence. As an example, a trained and qualified dentist might use hypnosis for hypnoanesthesia or hypnoanalgesia or for the allaying of anxiety in relation to specific dental work. Under no circumstances would it be proper for him to use hypnosis for the treatment of neurotic difficulties of his patient. The surgeon, obstetrician, anesthesiologist, gynecologist, internist, and general practitioner may legitimately utilize these techniques within the framework of their own particular field of competence.

A great deal has been said about the hazards of hypnosis, and this is still a controversial matter. One of the members of the conference, who is in a somewhat unique position since he has been consulted professionally by many colleagues who have utilized hypnosis and has also made a survey of results, presented material which indicated that in a number of patients there were harmful results which included the appearance of psychotic conditions and other complications. On the other hand, other consultants either personally or through correspondence indicated that they were not aware of any such harm resulting from the use of hypnosis. This is an area for further research.

Conclusions

General practitioners, medical specialists, and dentists might find hypnosis valuable as a therapeutic adjunct within the specific field of their professional competence. It should be stressed that all those who use hypnosis need to be aware of the complex nature of the phenomena involved.

Teaching related to hypnosis should be under responsible medical or dental direction, and integrated teaching programs should include not only the techniques of induction but also the indications and limitations for its use within the specific area involved. Instruction limited to induction techniques alone should be discouraged.

Certain aspects of hypnosis still remain unknown and controversial, as is true in many other areas of medicine and the psychological sciences. Therefore, active participation in high-level research by members of the medical and dental professions is to be encouraged. The use of hypnosis for entertainment purposes is vigorously condemned.

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WORK EFFORT AND THE DISABLED

CUMULATIVE clinical experience over the years has caused a considerable revision of thinking on the ability of the cardiac patient to continue working. In this issue of THE JOURNAL, page 147, Dr. Alvin Slipyan enriches the literature on this important subject with a report on the effect of work effort on the severely disabled cardiac patient in competitive industry. As he points out in the introduction to the article, despite all that has been written recently concerning employment and productivity of the person with cardiac disease, there has as yet been no controlled study to evaluate the effect of competitive industrial activity on the diseased heart.

As his conclusion points out this study of 19 employees, all classified as having severe or advanced heart disease, is unique in that never in the history of private industry has an organization adopted a deliberate policy of employing the "unemployable" person with cardiac disease. Members of the American Medical Association, however, are aware that their employer, Abilities, Inc., is a unique organization. In June, 1957, at its annual meeting in New York, the American Medical Association conferred its Citation for Outstanding Service upon Mr. Henry Viscardi Jr., the founder and president of Abilities, Inc. This was but the third time this high honor of the American Medical Association has been given. Since then many state medical societies have invited Mr. Viscardi to tell them more about Abilities, Inc., at their annual meetings.

Abilities, Inc., was founded in 1952 with four employees. It now employs over 300 persons, 65% of whom work from their wheel chairs. They earn an average hourly rate of $1.65 and the yearly payroll is over a half-million dollars. When compared with the national averages, their attendance and safety record is far superior. With original capital assets of $8,000, it now has assets of well over one million dollars. Dr. Slipyan's report is unique in that the 19 persons with cardiac disease previously considered "unemployable" help make this magnificent record of achievement.

Another interesting factor in this study is that it is part of a long-range research project being conducted by the research-education affiliate of Abilities, Inc., the Human Resources Corporation, with the aid of a grant from the Insurance Company of North America. The objective of this study is (1) to identify the physical, emotional, and social characteristics of severely disabled persons who have been unemployed for long periods of time or who have never had remunerative employment; (2) to evaluate what changes occur in these physical, emotional, and social characteristics when such severely disabled persons are placed in jobs commensurate with their abilities and in which they receive wages commensurate with those paid in regular industry for the same jobs; and (3) to see how these physical, emotional, and social characteristics compare with those of similarly disabled persons receiving public assistance and with those of other physically disabled persons employed in competitive industry and of nondisabled persons in competitive industry.

This is a large-scale, significant undertaking on which the Insurance Company of North America and Abilities, Inc., are to be congratulated, for it may change many of our present concepts on the employability of severely handicapped workers. This current report by Dr. Slipyan, which is but one of several disability categories to be studied, indicates, for example, that employment of persons severely disabled by cardiac disease may actually be beneficial.

It should be pointed out that these persons, as well as all the workers at Abilities, Inc., are not engaged in menial unskilled tasks. Most are highly skilled workers who were trained on the job and are operating extremely modern complex machinery. Parallel with the research being sponsored by the Insurance Company of North America, Abilities, Inc., is conducting another research project, aided by a grant from the Office of Vocational Rehabilitation, Department of Health, Education, and Welfare, on the ability of severely disabled persons to adjust to such complex machinery.

Probably the most unique aspect of the employment policies of Abilities, Inc., is that although it provides all of its disabled employees with complete periodic physical examinations these examinations are given after, not before, employment. This is done purposefully so that some of our present concepts of the physical demands of certain jobs can be tested clinically to prove or disprove their validity. Dr. Slipyan's provocative report raises serious questions concerning the validity of some of our present concepts, practices, and prejudices on employment of the person severely disabled by cardiac disease.

ORGANIZATION SECTION

STATEMENT OF THE A. M. A. BEFORE COMMITTEE ON VETERANS' AFFAIRS OF THE U. S. HOUSE OF REPRESENTATIVES BY RUSSELL B. ROTH, M.D., REGARDING NUMBER OF HOSPITAL BEDS TO BE AUTHORIZED IN VA FACILITIES

Mr. Chairman and Members of the Committee:

My name is Russell B. Roth, M.D., of Erie, Pennsylvania, where I am engaged in the private practice of medicine. I appreciate the opportunity of again appearing before your Committee. My last appearance was on March 5, 1957, when I represented the American Medical Association as a member of the Committee on Federal Medical Services. I appear again today as chairman of that committee.

My testimony today concerns the position of the American Medical Association with respect to the proper number of hospital beds which should be authorized in Veterans' Administration facilities for the care of war veterans—a question which is developed in some detail in House Committee Print No. 222. We have been especially interested in the study made by the Veterans' Administration, the Public Health Service, and the American Hospital Association, which is reported in that document, with its projections, through the year 1986, of the medical facilities required for veterans under various possible plans for future admissions.

Our Association holds one fundamental conviction on this subject. We believe that the Department of Medicine and Surgery of the Veterans' Administration has a single prime purpose—that of providing care for service-incurred or aggravated disease or disability. It was not created by Congress as an instrument of scientific research. It was not designed as a training ground for young doctors. And it was not intended as an agency for providing indigent medical care to the veteran population. It was developed for one purpose only—the provision of unstinting care for the war-injured.

And yet today any analysis of VA figures shows that service-connected medical care is a dwindling phase of VA operations. It is inevitable, as time separates us from the periods of actual combat, that there shall be even fewer cases of acute short-term service-connected illness, and that even these are likely to be acute episodes in the course of chronic disabilities. As the experience of the past is projected into the future it is apparent that service-connected care not only diminishes in volume but becomes overwhelmingly chronic in character. Even now something less than 15% of all new admissions to the VA are for service-connected care, and we suspect that most of these are re-admissions.

No one denies that the VA facilities are already greatly in excess of the requirements for service-connected care. It therefore follows that any further extension of VA medical operations can be justified only as an expansion of non-service-connected care. When Mr. Harvey Higley was VA Administrator he clearly stressed that point during your 1956 hearings. But what is the effect of this emphasis and concentration on non-service-connected care? It can only mean de-emphasis and dilution of service-connected care. There are many factors which must be considered. Who carries out the actual medical care in the Dean's Committee hospitals today—the experienced physician or the trainee? What class of patient commands the major attention of the teachers and the trainees in our VA hospitals today—the chronic, long-term inmates or the more dramatic, challenging, active problems that make up 85% of new admissions? What techniques are being employed in patient care—the conservative and well-tested, or the experimental techniques of research? Is the continuing care of the war-disabled veteran still truly of first magnitude concern to the VA, or has it dropped to a matter of third or fourth magnitude? We would ask your Committee to consider these questions critically.

Closely related to this problem is the whole subject of VA responsibility for care of non-service-connected disability. At the present time approximately 48%, almost half, of all veterans hospitalized for the care of non-service-connected disabilities are under VA auspices, and yet the studies of the Bradley Commission have shown that veterans in general are better off than non-veterans in respect to income, education, and level of employment. You have perhaps seen the lead article in the July issue of *Harper's* magazine by Mr. John E. Booth, himself a veteran, who comments "Veterans, who are now better off as a group than the rest of the population, will also be better off in their old age; they'll acquire more savings, private pension-plan payments, and other benefits than non-veterans." If this be true, and it seems reasonable in view of the all-out effort made by Congress and this Committee to aid the serviceman in his return to civilian life, how can it follow that nearly half of all veterans with non-service-connected conditions are in an "inability-to-pay" category entitling them to VA hos-

pitalization? And let us note that this is not a figure distorted by a preponderance of chronic tuberculous and neuro-psychiatric cases. The figure is 45% of the cases in the general medical and surgical classification. Mr. Booth, in the previously mentioned article, has as his thesis the view that such an unrealistic program subsidizes veterans who do not need it—"while the seriously disabled who do need it get short-changed."

In any event, Congress should surely determine its policy. Is it intended to furnish tax-paid federal medical care for all veterans who request it, and who are willing to indicate "inability to pay"? There are sizable waiting lists in this category, as you know. Future projections guarantee that as our wartime veteran population ages these lists will grow. If there should be an insistence on the part of Congress that the taxpayer actually is responsible for the care of disability unrelated to service, then there most assuredly is an obligation upon that Congress to define what constitutes "inability to pay." Today this is a matter of individual conscience. Mr. Booth refers to the affidavit on the 10-P-10 form as "something of a joke" because the law forbids the VA even to check up on it. Why should this be so? We would ask a sincere question: "Would this Committee permit the VA to grant a pension to a veteran without ascertaining his income level and his circumstances of need?"

What does the non-veteran do about the costs of illness? He buys insurance, or he pays in installments, or he meets the cost in other ways. If he really cannot afford hospitalization, the community pays for it. The A. M. A.'s Committee on Indigent Care has made a number of field studies on local and state medical care plans—a report of that Committee's studies occupies 90 pages of the record of your July 1953 hearings. This report does not disclose that there is even one welfare department in the country which will pay for a man's medical care purely on his unsupported statement that he cannot afford it.

We would respectfully suggest that this Committee authorize a serious study by the Government Accounting Office and the Veterans' Administration on the subject of income levels in NSC cases—primarily in the GM and S hospitals. We would further suggest strengthening of the law to permit examination of the admission affidavit which is so lightly considered in these times.

Now may we examine further the implications of this recent projection of future needs for VA hospital beds. The inexorable processes of nature furnish the patients. Medicine and its allied professions must provide the personnel. Congress must appropriate the funds for the mountains of brick and mortar which will be required to expand the facilities. And the taxpayer must produce the cash. It is certainly to the taxpayer's interest to know that his money is wisely spent. What will a million dollars of tax money do today in providing medical care? Our studies indicate that one million dollars in a Veterans' Administration GM and S hospital will care for 1,696 veterans. In a private GM and S hospital it would care for 5,389 patients—not veterans alone. It would include veterans wives, children, parents, friends and neighbors. Look at the same arithmetical problem in reverse. One-hundred n-s-c veterans receiving GM and S care in a VA hospital cost the taxpayer $58,953.00 while in a private non-federal general hospital the cost would be $18,572.00. We do not believe that throwing away nearly 70 cents out of every dollar spent on this medical care is a reasonable financial course for this nation.

We have dwelt largely on the problems of GM and S hospitals for a very real reason. It is our contention that the responsibility of government in various categories of illness must be defined. We submit that all non-service-connected illness in those unable to pay is the responsibility of government at the local community level. Chronic care for tuberculosis has traditionally been provided by the state government, acting for the communities, and this is probably true also in most neuropsychiatric disabilities. What then is the responsibility of the federal government to its disabled citizens be they veterans or non-veterans? This, we believe—needs definition. States for the most part can already meet the n-s-c needs in tuberculosis. As yet they cannot meet the neuropsychiatric needs and we will concede an interim period during which VA facilities which already exist may very appropriately be used. It is not, however, the responsibility of the federal government to operate a system of medical care for illness unrelated to military service in vicious competition with the private free-enterprise medical care system and the now well established insurance principles.

It has been alleged in correspondence between your Committee, the President, and the Administrator of the Veterans' Administration that there has been a reduction in VA hospital beds. This, we are convinced, is a bit of statistical sleight of hand. The accomplished daily patient load has increased annually to a present high of 111,740, and the average number of VA operating beds has similarly increased to a current peak of 121,257. By no criterion do these figures reflect any contraction in operation nor do they substantiate the statement which has been made that current policies being followed by the Veterans' Administration at the direction of the Bureau of the Budget are circumventing the policy for hospitalization of war veterans as established

by Congress. The alarming thing is that no contraction of operations seems to be anticipated. The Administrator of the VA reports an increase in operating beds in the next 18 months and an increased rate of construction of new facilities in the next fiscal year. Today, according to Mr. Whittier's figures, we have three times as many operating beds as service-connected patients. By 1956, according to the projections of the House Committee Print No. 222, we will have five times as many operating beds as service-connected patients—without building a single new bed. Already 75% of the tuberculous patients and 90% of the GM and S and neurological patients are being treated for non-service-connected conditions. The main function of the VA hospital system has become, in fact, if not in law or theory, the provision of non-service-connected care. The American Medical Association is not alone in deploring such an evolution. Two comprehensive studies of the Veterans' Administration have been made during recent years, both under chairmanship of persons of illustrious background and unassailable ideals of loyalty—General Omar Bradley and Mr. Herbert Hoover. Both studies have reached conclusions closely akin to our own. There is a grave responsibility in plotting a course which runs counter to the sound advice from these sources.

Finally, let us comment on the worth of our testimony. We are not asking for more jobs for physicians. We do not ask for more or larger fees. True—we have been accused by veterans organizations, and by the VA itself in times past, of a selfish interest in this subject. But let me assure you that if this were a conflict between the best interests of the patient-public and the vested interests of the medical profession the profession would inevitably yield to the public as it has on every occasion in the past. We ask not for an increase in VA medical jobs but for a decrease. We ask the federal government not to pay us for medical services to multitudes of patients whom we are prepared to serve without charge in our community hospitals. We do not think you can honestly find us insincere. We ask if you feel that the wartime wounded of our Armed Services—in the far-flung combat areas of Europe, the Pacific, and Korea received devoted and competent medical care at the time of their greatest need. If the answer is "yes," we would only point out that the physicians who provided these services, having passed in large numbers from service into civilian practice, are the ones who bring this testimony today. We who practice medicine are predominantly veterans, and we are also taxpayers, 100% of us.

In American medicine we may give our professional advice, but it is still up to the patient to decide whether this advice shall be followed or ignored. So it is here. We can only tell you, earnestly and sincerely, that in our considered judgment the veterans of this nation will be best served by a non-federal medical care system. We will pledge our assistance to you in every possible way in maintaining care for service-connected disability at the highest possible level. We will cooperate with you to the utmost in planning the complicated matter of returning non-service-connected care to the communities, where it properly belongs.

A. M. A. AWARD TO CBS

Arthur Hull Hayes, President of CBS Radio (center in photo), holds a plaque awarded to the CBS Radio Network by the American Medical Association for a special series of programs broadcast by CBS-owned Radio Station KCBS, San Francisco, to its 38 stations in the western network during the A. M. A.'s 107th Annual Meeting last June. Presenting the award is Dr. W. W. Bauer, Director of

Health Education for the A. M. A. (left), as Jules Dundes, Vice-president in charge of station administration for CBS Radio (right), looks on. The series, titled "Pulse of Medicine," featured a panel of doctors discussing various aspects of medicine and surgery.

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BUREAU OF MEDICAL ECONOMIC RESEARCH

NEW EXPERIMENTS TO PROVIDE VOLUNTARY HEALTH INSURANCE FOR RETIRED PERSONS

Walter Polner, Ph.D.

By the summer of 1957 it was estimated that 6 million persons aged 65 years and over had voluntary health insurance to pay for all or part of their hospital, surgical, and medical bills.[1] It is expected that this total coverage will rise, due to new experiments now being carried on by the Blue Cross and Blue Shield plans, as well as by the private insurance industry.

A large percentage of this coverage accrued from group enrollment. A recent (February, 1958) survey conducted by the Blue Cross Commission and the Blue Shield Medical Care Plans showed that over 3,500,000 persons are covered by these plans alone. Simultaneously, a series of additional experiments have been started by firms, associations, and welfare funds to provide such benefits to their ex-employees and members. It is this area of extension of benefits from group programs that may hold a major hope for additional coverage for the growing aged population in the near future.

The present situation is one of experimentation with the large majority of the new plans less than four years old. Pioneer plans such as the General Electric or Sears Roebuck experiments (10 and 8 years old, respectively) are considered old. However, the provision for conversion to individual policies has been a part of the basic Blue Cross and Blue Shield philosophy almost from their beginning; hence, the present large proportion of enrollment of the aged under these plans.

The new plans, both under Blue Cross–Blue Shield and commercial insurance auspices, have burgeoned in the last few years. Variations of Blue Cross and Blue Shield plans have been created; but, if any new significant trend has been created, it has been in the sharing of the cost of these plans by the employer for the employee after retirement and/or the adoption of extended benefit plans. Since March, 1957, the Schlitz, Miller, and Pabst brewing companies in Milwaukee have been paying 50% of the charges of Blue Cross and Blue Shield for their retired employees.

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Along with these trends under Blue Cross and Blue Shield plans, additional experiments have been undertaken by a variety of firms. While most of these plans are still new, some common characteristics are quickly perceived. These are as follows:

All are very young. Except for the Blue Cross plans, the majority have been implemented since the Korean war, such as the plans of the International Harvester Company, the Thompson Products Company of Cleveland, and the Argonne National Laboratory in Illinois.

They are primarily geared to treatment of the acute illness. Such plans as that of the Seiberling Rubber Company, providing 120 days per one continuous period of disability, are basically meeting the problems of the individual with an acute condition.

Not many persons have actually retired under these plans. It is the estimate of the United Rubber Workers that for all the large units in the rubber industry under their contracts only 7,500 employees have retired since the installation of the program.

Costs are still within the reasonable range contemplated at the origin of the plan. More than one administrator has commented that the plans have resulted in a performance much better than the companies had expected. This may be due to the fact that the persons retiring now under the plans have had a continuum of care under the plans while in employment and many diseases had been cared for earlier in life, or to the fact that in a period of high employment many persons have not retired and taken advantage of these plans.

The retired group under these plans are primarily in the age group 65 to 69, or still "young." This young part of the aged does not have an unreasonable utilization of such plans.

Many of these plans are tied into an automatic mechanism for payment. In some cases, in order for the individual to continue such hospital and medical coverage it is necessary to sign a prior authorization for deductions from the company pension payment, such as many plans now operating under Michigan Blue Cross.

Benefits are limited in one form or another. Although benefits for the active employees are limited normally by illness or annual limitations, most of

the new group plans limit the benefit to some maximum annual or lifetime amounts. Some plans eliminate maternity benefits or other extras.

firms is unknown. However, a recent survey of such provisions of firms with Blue Cross coverage in Michigan shows that the subsidy was 3½% of the

Selected Experiments Among New Group Plans

Name and Carrier	Benefits		
	Hospital	Surgical	Miscellaneous
Philadelphia Plant, American Viscose Corporation with Associated Hospital Service of Philadelphia and Travelers Insurance Company	120-Day comprehensive plan covers bed and board, including special diets; general nursing service; use of operating and treatment rooms and equipment; drugs and dressings; 30 days of hospital care during each contract year for mental and nervous conditions	$800 Standard Surgical Plan of Travelers Insurance Company	Unlimited laboratory tests; EKG; BMR tests; physical therapy; oxygen and oxygen therapy; x-ray examinations; administration of blood and blood plasma; intravenous injections and solutions
Harvard University Employees, Cambridge, Mass., with Blue Cross-Blue Shield	Covers hospital care in ward or semiprivate room; complete cost of first 15 days (on 16th day patient pays $6 per day toward cost of bill); use of operating room; laboratory tests; oxygen tents; x-ray services with necessary supplies and equipment; drugs and medications; appliances; blood and cost of administering transfusions	Covers all generally accepted operations and assisting and after-care for major operations; oral surgery, including regular extraction of 7 or more teeth	80% of charges for private duty nurse; 80% of charges for following services after $25 deductible during each calendar quarter: physician services for home and office visits, services of Visiting Nurses Association, prescription drugs, physical therapy by registered therapist, room and board up to $8 in nursing home or convalescent home, laboratory and pathology services, diagnostic x-ray services, blood or plasma; 60 days of hospitalization for mental illnesses or pulmonary tuberculosis; those with family income of $5,000 a year or less receive full coverage for medical, surgical, and anesthesia service by participating physician in Massachusetts; lifetime limits of $5,000 per person and maximum benefit per calendar year limited to $1,000 per person; on death of retired person, spouse may continue protection for period not to exceed 6 mo., after which spouse may apply for direct payment coverage with Massachusetts Blue Cross and Blue Shield.
Bird and Son, Inc., East Walpole, Mass., with Aetna Life Insurance Company	Up to $10 a day for first 60 days of hospitalization for retired employee and his dependent wife; all necessary hospital charges, other than charges for room and board, for first 60 days of confinement	$200	No benefits if confinement is due to pregnancy or resulting childbirth or miscarriage
Walker Manufacturing Company, Racine, Wis., with Blue Cross-Blue Shield plans	120 days for each hospitalization, including care for nervous and mental conditions in general hospitals (for latter conditions in nervous or mental institutions, up to $10 for 120 days of care for any one period of disability; such period shall be total duration of all sanatorium confinements separated by less than 180 days): benefits include semiprivate bed and board; general nursing care; use of operating room and delivery room; dressings; plaster casts and splints as provided by hospital; laboratory and BMR tests; x-ray examinations; EKG; physiotherapy; administration of blood and blood plasma; drugs; x-ray and radium therapy for proved malignancies, except those of skin	"Reasonable" charges made by attending physician	Outpatient benefits for administration of x-ray or radium therapy for proved malignancies except those of skin; "reasonable" charges for diagnostic x-ray and laboratory services; "reasonable" charges for attending physician during first 120 days of hospitalization per illness; home and office medical services; cost deducted from pension check of company; dependents can continue coverage under direct payment to Blue Cross and Blue Shield plans
Electrical Welfare Trust Fund, Washington, D. C., with Continental Casualty and Continental Assurance Companies	$15 a day for 31 days for retired employee or spouse; hospital extras, $300	$300	Physician services in hospital, home, or office; covers blood bank, x-ray procedures in and out of hospital; laboratory procedures; drugs; maternity benefits eliminated
General Tire and Rubber Company, Akron, Ohio, and Waco, Texas, divisions (hourly employees), with Equitable Life Assurance Society	120 days; covers semiprivate room for any one confinement	$250 surgical schedule	Special charges covered for miscellaneous hospital services; physician services in hospital up to 120 days
Central Hudson Gas and Electric Co., Poughkeepsie, N. Y., with Equitable Life Assurance Society	Major medical type; charges for hospital room and board up to $25 a day	Charges for diagnosis, treatment, and surgery	Private duty nursing by registered nurse; charges for local ambulance service, equipment, medication, appliances, x-ray service, laboratory tests, use of radium and radioactive isotopes, oxygen, blood and blood plasma, iron lung, physiotherapy and similar services, supplies, and treatment; must continue Blue Cross and Blue Shield at own expense in order to receive major medical benefits, consisting of payments of 75% of "covered charges" relating to each different accident or illness for employee or dependent up to $5,000 after payment of deductible; separate $5,000 maximum and separate deductible for each unrelated cause for each individual

There are subsidies of some sort. The employer may pay part of the cost. If the retired individual pays a group rate, part of his cost is borne through a higher group rate for active employees than that which they would otherwise pay. Of course, the exact extent and nature of this subsidy for most total premium which the active employees were charged in order to sustain the retired persons in their plan.[3]

The plans are subject to change. Many plans provide the same daily benefits for retired employees as for regular employees. As these plans

for active employees are changed, it is expected that the benefits for the retired workers will be changed. However, many companies are still experimenting with the type of plan they will use. As they obtain more experience they will modify their plans accordingly.

Many plans cover only retirements effective after the plan has been instituted. In addition, only those with some length of seniority have all the benefits, as under the plan of the Carrier Corporation.

There are limited statistical data. In many cases, companies have not established special statistical tabulations due to the smallness of the samples involved.

Comment

While these patterns are easily seen in the study of plans now available, they have not answered the fears of many employers on the cost problems raised by such coverage. In a survey made by Michigan Blue Cross, the range of guesses as to future costs runs from 2 to 10 times [3] as much for utilization of hospitals by the aged.

There is no doubt that if persons now in the aged group have voluntary health insurance they will use hospital and medical care more than those below 65 years of age.[4] The recent study published by the New York State Insurance Department showed that the average days of confinement for males per person per year under a 120-day benefit insurance contract at 25 years of age is 0.53 days; at 55 it is 1.5 days; at 65 it is 2.43 days; at 75 it is 3.66 days; and at 85 it is 6.27 days.

Older persons utilize the plans to a greater extent. The fact is that all persons have become more accustomed to using the hospitals. General hospitals have changed their role. They no longer care for only the critically ill but now also provide an elaborate diagnostic facility as well as care for the mentally ill and others with illnesses previously handled in the home or the doctor's office.

The very nature of the insurance policy will encourage additional use of hospitals. In the recent survey of the New York State Insurance Department it was shown that there was more utilization under a 120-day hospital policy than under a 31-day policy.[4]

Advances have been made in medical science which make it possible to treat successfully many conditions formerly regarded as hopeless. However, these medical advances also serve to cut the length of stay in the hospital or in bed at home.

There has been inflation of the cost of health care over the past decade. Hospital costs seem to be rising at the rate of 5% per annum.[5] Planning for a lifetime protection must consider costs in the future.

There is greater availability and excellence of hospital facilities to be used. Under the Hill-Burton Act alone over 115,000 additional hospital beds have been built since 1948. Substantial facilities also have been built during these years outside the Hill-Burton program.

For companies planning a program of benefits tailor-made to the needs of their employees, the answers to many questions are unknown quantities. Since they do not have enough information to make a reasonable guess, they will make no guess. They fear the future. Unfortunately, fear is one of the most difficult human emotions to deal with.

In spite of all of these questions, more and more companies, either because of their belief in the need for such programs or due to collective bargaining pressure, have experimented with bold new programs. In this fast-changing situation plans have evolved in an attempt to answer the needs of retired employees. Certainly, not all necessary information has been obtained, but if all companies were to wait for all necessary information, action would never be forthcoming. These experiments may give the elements of basic information needed to formulate patterns for the more timid firms.

Some selected experiments are listed in the table. In every case these experiments have been created in spite of lack of absolute knowledge as to future costs. More experiments are being undertaken every day by companies or fund administrators or trustees. There has been no one single answer produced for the many aspects of financing medical, hospital, and surgical care for the aged. These answers have been provided by those firms who are willing to take a calculated risk. Perhaps the best philosophy for other firms is that of Mr. Justice Brandeis, who stated, "If we would guide by the light of reason, we must let our minds be bold." It is reasonable and proper for the aged to have voluntary health insurance. All that is needed is a bit more acceleration of boldness.

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MEDICAL NEWS

CALIFORNIA

Annual Postgraduate Assembly in Santa Monica.—The 10th annual Postgraduate Assembly sponsored by Saint John's Hospital will be held Sept. 11-13, 1958. Guest speakers will be Drs. Brian D. Best, obstetrician, Winnipeg, Canada; Dr. John D. Camp, radiologist, Los Angeles; Dr. Lester R. Dragstedt, surgeon, Chicago; Dr. John W. Pender, anesthesiologist, Palo Alto; Dr. Albert M. Snell, internist, Palo Alto; and Dr. Sheldon C. Sommers, pathologist, Boston. Dr. John C. Eagan, Los Angeles, is founder and director of the Postgraduate Assembly. All sessions will be held at Saint John's Hospital, Santa Monica.

Personal.—The University of California at its 95th commencement at Berkeley, conferred an honorary degree of doctor of laws upon Dr. Robert T. Legge, professor of hygiene emeritus. Dr. Legge, who served two terms on the Council of Industrial Health, American Medical Association, was the recipient of the W. S. Knudsen award for the "most outstanding" contributions to industrial medicine (1951).——Dr. Joseph J. Downing, formerly acting director of the New York State Mental Health Research Unit in Syracuse, has been appointed program chief of the Mental Health Section of the San Mateo, California, County Department of Health and Welfare.

New Genetics Department at Stanford.—Joshua Lederberg, Ph.D., chairman, department of medical genetics, University of Wisconsin School of Medicine, Madison, has been named to head a new department of genetics at Stanford University School of Medicine, effective in April, 1959. Dr. Lederberg, who has also served as a visiting professor at the universities of California and Melbourne, Australia, is a member of the National Academy of Sciences and a consultant to the National Institutes of Health. Establishment of the new department of genetics, as well as of a new department of biochemistry, is a move toward integration of the medical school with the university. Stanford Medical School is now located in San Francisco. By the fall of 1959 it will occupy a new 22-million-dollar medical center on the campus near Palo Alto.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

FLORIDA

University Grants.—The University of Miami School of Medicine, Coral Gables, has received a grant of $129,000 from the U. S. Public Health Service for scientific equipment for its new research building, to be completed in late 1959. The new eight-story structure will cost over 2 million dollars.——Two grants totaling $107,000 have been received by the University of Florida College of Medicine, Gainesville, both made by the National Institutes of Health. Dr. Samuel P. Martin, head, department of medicine, received a grant of $82,000 for a five-year study of human leukocytes. An additional grant of $25,000 was made by the NIH to support undergraduate cardiac training of medical students, the third year this grant has been renewed. It will be administered by Dr. William J. Taylor, assistant professor of medicine.

ILLINOIS

Ophthalmology and Otolaryngology Meeting in Springfield.—The 31st annual meeting of the Central Illinois Society of Ophthalmology and Otolaryngology will be held in Springfield Sept. 19-21. Guest speakers will include Drs. Louis J. Feit, New York City (otolaryngology), and Ichiro D. Okamura, Boston (ophthalmology). The society speakers will be Drs. Louis R. Kent, Champaign, in ophthalmology, and Grover C. Otrich, Belleville, in otolaryngology. The night of Sept. 19 Dr. S. Glidden Baldwin, of Danville, will be the speaker. For information write Dr. Clarence A. Fleischli, Secretary-Treasurer, Central Illinois Society of Ophthalmology and Otolaryngology, 520 E. Allen St., Springfield, Ill.

Chicago

Home for Incurables Affiliates with University of Chicago.—The Chicago Home for Incurables and the University of Chicago have entered into an affiliation by which the home is to construct a new hospital adjacent to the University Clinics and become a model center for study and treatment of chronic illness, with special emphasis on older age groups. The home will use 1.5 million dollars of its funds to build the new hospital, which will be three stories and basement, and the university will provide the medical and specialized services which will enable the home to render an active program of treatment and rehabilitation. The Chicago Home for Incurables was established by the will of Clarissa Park of Chicago, who died in 1885. The home

was incorporated on Dec. 20, 1886, and opened its main building in 1890. A majority of the patients pay partial costs of their maintenance.

Prize for Investigation in Medicine.—The Institute of Medicine of Chicago is offering an annual prize of $300 for the most meritorious investigation in medicine or in the specialties of medicine. The investigation may be in the fundamental sciences, provided the work has a definite bearing on some medical problem. Competition for 1958 is open to graduates of Chicago medical schools who completed their internship or one year of laboratory work within a period of five years prior to Jan. 1, 1958, excluding their terms of service in the Armed Forces. Manuscripts must be submitted to the Secretary of the Institute of Medicine of Chicago, 86 E. Randolph St., Chicago 1, not later than Dec. 31. The prize paper will become the property of the institute. If no paper submitted is deemed worthy of the prize, the award may be withheld at the discretion of the board of governors.

Program for University of Illinois Expansion.—A $32,500,000 program for the construction of eight new buildings and rehabilitation of older ones was presented July 29 to the board of trustees for the University of Illinois Professional Colleges in the Medical Center District on Chicago's west side. An appropriation of $6,724,000 will be sought in the next General Assembly to initiate the program during 1959-61. It is part of a 10-year building plan for the entire university. The colleges of dentistry, medicine, pharmacy, a school of nursing, a 620-bed general hospital and a division of the graduate college form the nucleus of the university's professional colleges. Major elements of the building program are as follows:

Medical Research Laboratory; Medical Sciences Building; Enlargement of the University of Illinois Hospitals; Library—Basic Science Building: A new building is planned to house the university's Library of Medical Sciences; Auditorium—Gymnasium; Physical Plant Service Building; Drug and Horticultural Experiment Station; Classroom—Office Building.

Personal.—Dr. Heinz Grunze, co-chairman of the department of medicine at the Free University of West Berlin, will begin a one-year fellowship at the University of Chicago medical and biological research center on Sept. 1, under a $3,600 grant from the American Cancer Society. He also will lecture in the university's School of Medicine on thoracic cytology.——Dr. Murray Rabinowitz of the Rockefeller Institute for Medical Research has been appointed director of the new cardiopulmonary laboratory of the University of Chicago Clinics.——Dr. Heinz Kohut, secretary, Chicago Psychoanalytic Society, was appointed professorial lecturer in the department of psychiatry at the University of Chicago, effective July 1. Dr. Kohut, who received his doctor of medicine degree from the Medical School of the University of Vienna, Austria, has been on the teaching faculty of the Chicago Institute for Psychoanalysis since 1953.——Dr. Bernard J. Michela has been appointed director of the Rehabilitation Institute of Chicago, succeeding Dr. Joseph H. Chivers, who was elected to the board of directors following his resignation from the post he had held since 1955.

KENTUCKY

Annual State Meeting in Louisville.—The Kentucky State Medical Association's annual meeting will be held Sept. 23-25 at the Columbia Auditorium, Louisville. Two panel discussions are planned, "The Pregnant Patient" and "Geriatrics and Surgery," moderated by Drs. Frank R. Lock, Winston-Salem, N. C., and Rattig A. Griswold, Louisville, respectively. Dr. Edward B. Mersch, of Covington, president of the association, will present an address the morning of Sept. 23. Thirteen specialty groups will meet simultaneously the afternoon of Sept. 24. At the presidents luncheon (11:50 a. m., Sept. 24) Clarence Manion, J.D., South Bend, Ind., will present "The Disease Called Despotism." Scientific exhibits are planned. For information write Mr. J. P. Sanford, Executive Director, Kentucky State Medical Association, 1169 Eastern Parkway, Louisville 17, Ky.

MICHIGAN

Building for Industrial Medicine.—Construction of an $800,000 Industrial Medicine and Hygiene Building began Aug. 18 at Wayne State University College of Medicine, Detroit. Radiation studies will be conducted on two specially designed and equipped floors of the four-story building. According to Dr. Gordon H. Scott, dean of the college, research to be conducted in the building will include study of atmospheric pollutants, including radioactive substances, and vehicular health hazards as they may attend certain occupations. A special area for electronic instrumentation will be installed, and a laboratory for study of exhaust fumes will be on the first floor.

MISSOURI

Dr. Gelperin Appointed Health Director.—In a reorganization of the city health division of Kansas City, Dr. Abraham L. Gelperin, of Chicago, was named director of health and hospitals, effective August 1 to succeed Dr. Hugh L. Dwyer, who became director of public health services.

NEVADA

Annual State Meeting in Elko.—The 55th annual meeting of the Nevada State Medical Association will be held Sept. 17-20 in Elko. A panel discussion on anesthesiology will be moderated by Dr. Charles

F. McCuskey, head, department of anesthesiology, University of Southern California School of Medicine, Los Angeles. The program includes the following out-of-state speakers: Drs. Wallace S. Brooke, Paul D. Hoeprich, and Scott M. Smith, Salt Lake City, Utah; John B. Dillon, Los Angeles; Lowell A. Rantz and Victor Richards, San Francisco; and Abe Ravin, Denver. Mr. Roland F. Logan, Los Angeles, will be the guest speaker at the annual banquet Sept. 18. A golf tournament and ladies' program are arranged. For information write the Nevada State Medical Association, P. O. Box 118, Reno, Nevada.

PENNSYLVANIA

Address on Conquest of Space.—Temple University School of Medicine, Philadelphia, will hold a special convocation, Oct. 23, at which Wernher von Braun, Ph.D., will present an address at 10:30 a. m. at the Dental-Pharmacy Auditorium, 3223 N. Broad St., on "The Conquest of Space." Dr. von Braun, who is director of the Development Operations Division of the Army Ballistics Missile Agency at Huntsville, Ala., will be awarded an honorary degree of doctor of science at this time. On the same day, at 2:45 p. m., at the ninth annual Military Medico-Dental Symposium on Space Medicine at the U. S. Naval Hospital in Philadelphia, Dr. von Braun will again speak on the same subject.

Philadelphia

University Grant.—A health research facilities grant of $46,038 to The Woman's Medical College of Pennsylvania has been approved by the U. S. Public Health Service, and will be used toward the purchase of the scientific equipment for the college's 2-million-dollar Research Wing, to be constructed this fall. The college's development program, under the chairmanship of Mrs. John B. Kelly, vice-president of the board of corporators, has a goal of 4 million dollars.

SOUTH DAKOTA

General Practice Meeting in Huron.—The annual meeting of the South Dakota Chapter of the American Academy of General Practice will be held Sept. 19-20 at the Marvin Hughitt Hotel, Huron. A total of 24 papers are scheduled for presentation, including anatomy of the hand and forearm, by Walter L. Hard, Ph.D., dean, University of South Dakota School of Medical Sciences, Vermillion. Dr. Arthur A. Lampert, of Rapid City, president of the association, will discuss clinical fluid balance problems the morning of Sept. 20. Round-table discussions will conclude each day's program.

WISCONSIN

Dr. Kersting Succeeds Dr. Foerster.—Dr. David W. Kersting has been appointed professor and chairman of the department of dermatology at Marquette University School of Medicine, Milwaukee, succeeding Dr. Harry R. Foerster, who becomes clinical professor emeritus Aug. 15. Dr. Kersting is the director of graduate training in dermatology at the Veterans Administration Hospital at Wood and at Marquette, and chief of the dermatology and syphilology sections at Wood. He will direct undergraduate teaching and research at the medical school.

GENERAL

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	Aug. 16, 1958: Paralytic Type	Aug. 16, 1958: Total Cases	Aug. 17, 1957 Total
New England States			
Maine	..	..	..
New Hampshire	..	1	..
Vermont	..	..	..
Massachusetts	..	1	..
Rhode Island	1	1	..
Connecticut	..	2	1
Middle Atlantic States			
New York	12	19	5
New Jersey	5	17	5
Pennsylvania	5	6	3
East North Central States			
Ohio	3	14	17
Indiana	1	3	19
Illinois	4	7	20
Michigan	20	42	47
Wisconsin	1	3	22
West North Central States			
Minnesota	1	1	2
Iowa	..	4	8
Missouri	4	5	10
North Dakota	2	2	..
South Dakota	..	..	4
Nebraska	..	..	3
Kansas	1	1	5
South Atlantic States			
Delaware	..	4	..
Maryland	1	1	..
District of Columbia	..	..	7
Virginia	6	7	2
West Virginia	3	5	2
North Carolina	3	12	19
South Carolina	..	..	4
Georgia	1	3	6
Florida	1	1	..
East South Central States			
Kentucky	1	1	7
Tennessee	1	7	7
Alabama	6	6	2
Mississippi	2	10	5
West South Central States			
Arkansas	..	3	1
Louisiana	2	3	6
Oklahoma	..	1	5
Texas	16	22	21
Mountain States			
Montana	5	5	..
Idaho	..	1	1
Wyoming	..	..	1
Colorado	1	1	..
New Mexico	..	..	6
Arizona	..	1	2
Utah	..	1	..
Nevada	..	..	..
Pacific States			
Washington	..	1	1
Oregon	..	1	..
California	5	7	28
Territories and Possessions			
Alaska	..	..	..
Hawaii	5	5	..
Puerto Rico	..	..	4
Total	119	238	318

Annual Meeting of Vermont and New Hampshire Societies.—The ninth annual combined meeting of the Vermont State Medical Society and the New Hampshire Medical Society will be held Sept. 19-22 at the Mount Washington Hotel, Bretton Woods,

N. H. The general sessions will have the following themes: communications, rehabilitation (two), and trauma, with Drs. Arthur W. Burnham, president, New Hampshire Medical Society, James P. Hammond, president, Vermont State Medical Society, Clinton R. Mullins, president-elect, New Hampshire Medical Society, and Wayne Griffith, president-elect, Vermont State Medical Society, presiding. Out-of-state speakers include the following: Louis M. Lyons, L.H.D., and Drs. William Malamud, Paul M. Zoll, William V. McDermott Jr., Sara M. Jordan, Joe V. Meigs, Siegfried J. Thannhauser, Frank C. Wheelock Jr., and John L. Tullis, Boston; James W. Rae Jr., Ann Arbor, Mich.; Alvan L. Barach, New York City; and William F. Croskery, Brookline, Mass. Speaker at the the annual banquet, 7 p. m., Sept. 20, will be Richard D. Weigle, Ph.D., president of St. John's College, Annapolis, Md., who will present "Education: Appraisal and Prognosis." Entertainment includes a golf tournament Sept. 19. Exhibits and a ladies' program are arranged. For information write Dr. Warren H. Butterfield, Secretary-Treasurer, New Hampshire Medical Society, Concord, N. H.

Award for Investigations in Psychiatry.—The Society of Biological Psychiatry is offering an annual award which was made possible by the A. E. Bennett Neuropsychiatric Research Foundation. The award will consist of traveling expenses to the annual meeting plus expenses at the meeting, in addition to an honorarium of $250. It will preferably be given to a young investigator and not necessarily a member of the society for work which has been recently accomplished and not published. Papers should be submitted in quadruplicate to Arthur A. Ward, School of Medicine, University of Washington, Seattle 5, Wash., or to Dr. Harold E. Himwich, Chairman, Committee of Award, Galesburg State Research Hospital, Galesburg, Ill. Deadline for manuscripts is April 30, 1959.

Society News.—Officers of the **American Therapeutic Society** for 1958-59 are: president, Dr. Tom D. Spies, Birmingham, Ala.; vice-presidents, Drs. George E. Burch Jr., New Orleans, George C. Griffith, Los Angeles, and Frank B. Kelly, Chicago; secretary, Dr. Oscar B. Hunter Jr., 915-19th St. N. W., Washington, D. C.; and treasurer, Dr. Joseph A. Davis, Chicago.——The following officers of the **American College of Chest Physicians** have been elected for the year 1958-1959: president, Dr. Donald R. McKay, Buffalo, N. Y.; president-elect, Dr. Seymour M. Farber, San Francisco; first vice-president, Dr. Mathew J. Flipse, Miami; second vice-president, Dr. Hollis E. Johnson, Nashville, Tenn.; treasurer, Dr. Charles K. Petter, Waukegan, Ill.; assistant treasurer, Dr. Albert H. Andrews Jr., Chicago; chairman, board of regents, Dr. John F. Briggs, St. Paul; and historian, Dr. Carl C. Aven, Atlanta, Ga.

Program for Medical Research.—The National Fund for Medical Education has established a Medical Research Program through which contributions from united funds, community chests, voluntary health agencies, and other organizations will be channelled into basic research, to "help advance the search for basic medical knowledge . . . encourage the training of research personnel [and] help the nation's medical schools and other qualified institutions maintain a proper balance between basic and 'project, or applied, research.'" Fund grants are unrestricted but are used primarily for support of teaching budgets of the medical schools. Details of the new program have been worked out by a committee including Dr. Vernon W. Lippard, dean, Yale University School of Medicine, as chairman. The National Fund for Medical Education was formed in 1949 under the leadership of President Dwight D. Eisenhower, then president of Columbia University; former President Hoover, who is honorary chairman of the fund's board of trustees; educators, university presidents, and prominent business leaders. The fund recently awarded $3,178,825 to the medical schools, bringing to $15,843,766 the total awarded since its first grants were made in 1949.

Medical History Essay Contest.—The William Osler Medal of the American Association for the History of Medicine is awarded annually for the best unpublished essay on a medico-historical subject written by a student in one of the medical schools of the United States or Canada. This medal commemorates the great physician, Sir William Osler (1849-1919). Essays submitted should not exceed 10,000 words in length, and should demonstrate either original research or an unusual understanding of a medico-historical problem. It is expected that the student will seek help only from faculty advisors and from sources open to all investigators, such as libraries and museums. The prize-winning essay may be considered for publication in the *Bulletin of the History of Medicine*, the official organ of the association. All students are eligible and may submit essays at any time up to the next entry date after graduation. The next entry date terminates April 1, 1959. Essays should be submitted to Dr. Samuel Radbill, 7043 Elmwood Ave., Philadelphia 42.

Meeting on Anesthesiology in Vermont.—The first regional conference of the New England Society of Anesthesiologists will be held Sept. 18-19 at the Equinox House, Manchester-in-the-Mountains, Vermont, under the theme "Old and New Problems in Anesthesia." Keynote speaker will be Dr. Eman-

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uel M. Papper, professor of anesthesiology, Cornell University Medical College, New York City. Five papers will be presented at each of the two sessions. Technical exhibits are planned. Entertainment includes a golf tournament and the annual banquet Sept. 19, 7:30 p. m. Registration fee for nonmembers is $5. For information write Dr. Thomas K. Burnap, Secretary, New England Society of Anesthesiologists, 721 Huntington Ave., Boston 15.

Conference on Electrical Techniques in Medicine.—The 11th annual Conference of Electrical Techniques in Medicine and Biology will be held in the Nicolett Hotel, Minneapolis, Nov. 19-21, sponsored by the American Institute of Electrical Engineers, the Institute of Radio Engineers, and the Instrument Society of America. Theme of the meeting is "Biology and Computers." One special session will be on the possibility of applying electronic computers to the theoretical and clinical problems of electrocardiography. The session will examine the ways in which a physician can be aided in making rapid and accurate diagnosis through the use of electronic computers. Another session will be devoted to computer ideas as applied to electroencephalography, and a third special session will be on the inverse problem of developing computer application on the basis of biological coding, biological transducer designs, and biological logic. The meeting is open to all scientists, engineers, and physicians. For information write The American Institute of Electrical Engineers, % Raymond C. Mayer & Associates, 36 W. 46th St., New York City 36.

Meeting of American Medical Colleges in Philadelphia.—The 69th annual meeting of the Association of American Medical Colleges will be held Oct. 13-15 at the Sheraton Hotel, Philadelphia. The presidential address, "The Problem of Change," will be given by Dr. Lowell T. Coggeshall, Chicago. A panel discussion, with James B. Conant, Litt.D., Boston, presiding, will be held on "Medical Education and the University." Dr. Gunnar Gundersen, President, American Medical Association, will present "AMA and the Medical School Partnership." Papers by foreign participants are: "Graduate Medical Education in Europe," by Dr. John P. Sandblom, Lund, Sweden, and "The Dalhousie Postgraduate Program: An Experience in Continuing Medical Education," by Dr. Lea C. Steeves, Dalhousie University, Nova Scocia, Canada. At the annual dinner, Oct. 13, 7 p. m., Dr. Conant will give the first Alan Gregg Lecture. For information write the Association of American Medical Colleges, 2530 Ridge Ave., Evanston, Ill.

Medical Scientists Visit Soviet Union.—Three American medical scientists started a visit in the Soviet Union Aug. 11 in a new exchange program sponsored by the American Friends Service Committee. They are Dr. Joseph Stokes Jr., Philadelphia; Dr. George A. Perera, New York City; and Samuel A. Corson, Ph.D., Little Rock, Ark. The group traveled in the Soviet Union until Sept. 9. The project, undertaken by the Quaker Organization, was arranged in cooperation with VOKS (Union of Soviet Societies for Cultural Relations with Foreign Countries) and the Soviet Embassy in Washington. The three men attended sessions of the International Congress for Microbiology in Stockholm before going to the Soviet Union. After leaving Russia they stopped in Poland for visits with Polish doctors and scientists. Dr. Stokes is president of the American Pediatric Society, professor of pediatrics at the University of Pennsylvania School of Medicine, and physician-in-chief of Children's Hospital. Dr. Perera is a member of the American Board of Internal Medicine, professor of medicine at the College of Physicians and Surgeons of Columbia University, and chairman of Friends Medical Society. Dr. Corson, who speaks fluent Russian, is associate professor of physiology and pharmacology at the University of Arkansas School of Medicine. The American Friends Service Committee is a world-wide Quaker peace and human welfare agency, with a national office in Philadelphia and 11 regional offices in the United States. It has programs in more than a dozen foreign countries.

FOREIGN

Cholera Outbreak in Nepal.—Cholera has broken out in Khatmandu, capital of Nepal, the first cholera epidemic to strike this Himalaya mountain nation in over half a century, according to word received at World Health Organization headquarters. At the request of the Government of Nepal, WHO is supplying 25,000 doses of vaccine to help immunize the population. Cases and deaths are twice as numerous as last year in India and East Pakistan, and an epidemic has struck Thailand for the first time in many years. Cholera has also been recorded in Cambodia and Burma. Cumulative totals for 1958 are, as of 31 July:

	Cases	Deaths
India	29,372	12,851
East Pakistan	10,386	6,644
Thailand	8,964	1,190
Cambodia	3	0
Burma	4	2
	48,729	20,687

Any person coming from an infected area, whether or not he is in possession of a vaccination certificate against cholera, may be placed under surveillance for a maximum of five days. If the traveller is not in possession of such a certificate, he may be placed in isolation for the five-day period.

CORRECTION

Appoint Dr. Wagner to Cardiovascular Research Chair.—Concerning an item published under this title in medical news Aug. 9, page 1854 of THE JOURNAL, in which it is stated that Dr. Bernard M. Wagner will be assistant professor of pathology at the University of Washington, Seattle, Miss Elizabeth J. Dictor, librarian, the Children's Hospital of Philadelphia, where Dr. Wagner was pathologist, has written that "Dr. Bernard M. Wagner will be associate professor."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 20, 1958. *Oral.* Chicago, Oct. 13-16. *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application is Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application is Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. No application can be accepted after that date. It should be noted by prospective candidates that the deadline date in 1959 is August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written,* qualifying test (Part I), January 1959. Final date for filing application was July 1, 1958. *Oral Examinations* 1958 (Part II): Chicago, Oct. 6-10. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Chicago, Oct. 9-11. Final date for receipt of case reports was July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PREVENTIVE MEDICINE: *Examination in Public Health.* St. Louis, Oct. 24-26. Final date for filing application was Aug. 15. Sec., Dr. Thomas F. Whayne, 3438 Walnut St., Philadelphia 4.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Regular Examination.* Washington, D. C., Dec. 8-11. Final date for filing application was July 1. *Special examination in Nuclear Medicine for those diplomates in Radiology or Therapeutic Radiology.* Washington, D. C., Dec. 6. Final date for filing application is Oct. 1. *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application is Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Philadelphia, Sept. 15-16; Rochester, Minn., Oct. 20-21; Nashville, Tenn., Nov. 17-18; New York City, Dec. 15-16; Houston, Tex., Jan. 12-13; New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: Various centers throughout the United States. *Written.* Spring of 1959. Final date for filing application is December 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Avenue, Detroit 2.

AMERICAN BOARD OF UROLOGY: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

DEATHS

Adams, Jesse Lee Jr., Reno, Nevada; Georgetown University School of Medicine, Washington, D. C.; 1898; died in St. Mary's Hospital July 16, aged 83, of coronary occlusion.

Alexander, Horace Knox Ⓜ Fayetteville, Tenn.; University of Nashville (Tenn.) Medical Department, 1909; served overseas during World War I; died in the Lincoln County Hospital July 15, aged 72, of cerebrovascular accident.

Allum, Arthur Wesley, Glendale, Calif.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1903; specialist certified by the American Board of Obstetrics and Gynecology; an associate member of the American Medical Association; served as president of the Glendale Branch of the Los Angeles County Medical Association; fellow of the American College of Surgeons; on the staff of the Memorial Hospital; died in St. John's Hospital, Santa Monica, July 20, aged 78, of myocardial infarction and coronary thrombosis.

Branch, Frederick Douglas, Binghamton, N. Y.; Albany (N. Y.) Medical College, 1899; an associate member of the American Medical Association; served on the staffs of the Binghamton City and Binghamton State hospitals; died July 19, aged 84.

Brenner, Edward Christopher, New York City; Columbia University College of Physicians and Surgeons, New York City, 1908; member of the founders group of the American Board of Surgery; member of the Medical Society of the State of New York; fellow of the American College of Surgeons; formerly chairman of the medical board of the New York City Department of Correction; at one time associate professor of clinical surgery at New York Post-Graduate Medical School; served on the staffs of the Midtown and Riker's hospitals; died in Butler, Pa., July 24, aged 73.

Bunge, Charles Albert, Bland, Mo.; Barnes Medical College, St. Louis, 1910; past-president of the Gasconade County Medical Association; formerly mayor, school board member, and county coroner; died July 22, aged 79, of heart disease.

Burner, Allen Eugene, Durbin, W. Va.; College of Physicians and Surgeons, Baltimore, 1908; died July 23, aged 81, of a heart attack.

Butz, Joseph Aaron, Los Angeles; Bennett Medical College, Chicago, 1902; died July 15, aged 80, of coronary disease and arteriosclerosis.

Ⓜ Indicates Member of the American Medical Association.

Carbonell, Arturo Ⓜ Colonel, U. S. Army, retired, Arlington, Va.; Jefferson Medical College of Philadelphia, 1911; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; service member of the American Medical Association; veteran of World Wars I and II; entered the regular Army in 1917 and retired Aug. 31, 1948; chief of the medical service at West Point for many years; died in the Walter Reed Army Hospital, Washington, D. C., July 16, aged 69, of acute myocardial infarction.

Conner, Elwin Iris, Pomona, Calif.; University of Nebraska College of Medicine, Omaha, 1926; at one time a medical missionary in West Africa; veteran of World War II; hanged himself July 20, aged 60.

Crosby, Roy Campbell Ⓜ Boise, Idaho; Tufts College Medical School, Boston, 1944; certified by the National Board of Medical Examiners; in the military service from Feb. 1, 1954, to Nov. 19, 1955; associated with St. Luke's and St. Alphonsus hospitals; died in Marlboro, Mass., July 20, aged 39, of injuries received in a private plane crash.

de Steiguer, John Rodolph Ⓜ San Marcos, Texas; Hospital College of Medicine, Louisville, Ky., 1890; died May 8, aged 88, of cancer.

Devine, Winifred Morrill Woolls, Lowell, Mass.; Boston University School of Medicine, 1908; retired school physician for the city of Lowell; died July 18, aged 78, of coronary thrombosis.

Dimmitt, Egbert King Ⓜ Farmington, Ill.; University of Louisville (Ky.) Medical Department, 1909; vice-president of the Bank of Farmington; charter member and past-president of the Farmington Rotary Club; associated with the Graham Hospital in Canton and the Methodist Hospital of Central Illinois in Peoria, where he died July 4, aged 75, of arteriosclerotic heart disease.

Dorsey, George Hamilton Ⓜ Major, U. S. Army, retired, Wheat Ridge, Colo.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1915; service member of the American Medical Association; member of the American Urological Association; entered the regular Army in 1918 and retired Dec. 15, 1922; died in Reno, Nevada, July 6, aged 65, of congestive heart failure and pneumonitis.

Edstrom, Henry, Springfield, Ill.; University of Minnesota Medical School, Minneapolis, 1926; specialist certified by the American Board of Radiology; member of the American College of Radi-

ology; veteran of World War II; died July 17, aged 58, of acute coronary occlusion and myocardial infarction.

Ekwurzel, George Macy ⊗ Colonel, U. S. Army, retired, San Francisco; University of Pennsylvania Department of Medicine, Philadelphia, 1897; service member of the American Medical Association; fellow of the American College of Surgeons; entered the regular Army in 1901 and retired May 31, 1939; veteran of World War I; died in the Letterman Army Hospital June 21, aged 83.

Eyestone, Fred Levi ⊗ Toledo, Ohio; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1916; fellow of the American College of Surgeons; veteran of World War I; served on the staffs of the Toledo, Riverside, and St. Vincent's hospitals, and the Mercy Hospital, where he died July 20, aged 65, of cancer.

Gibson, Stewart Merrill ⊗ Southbridge, Mass.; Tufts College Medical School, Boston, 1928; on the staff of the Harrington Memorial Hospial; died in Sturbridge July 16, aged 54, of coronary thrombosis.

Goldenberg, Marcellus ⊗ New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1926; specialist certified by the American Board of Internal Medicine; assistant clinical professor of medicine at the Columbia University College of Physicians and Surgeons; credited with having discovered the presence of nor-epinephrine in the adrenal gland; associated with the Presbyterian Hospital, where he died July 30, aged 57, of myocardial infarction.

Gordon, Charles Howard ⊗ Portland, Maine; Medical School of Maine, Portland, 1919; specialist certified by the American Board of Otolaryngology; past-president of the Cumberland County Medical Society; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; consultant at the Webber Hospital in Biddeford; on the staffs of the Maine General Hospital and the Maine Eye and Ear Infirmary, where he was chief of the ear, nose and throat service; died July 28, aged 64, of ruptured aortic aneurysm.

Haines, Charles Tomlinson, Ambler, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1898; died in Doylestown July 22, aged 86, of adenocarcinoma of the prostate and arteriosclerosis.

Herzon, Herbert, San Francisco; born in Chicago Jan. 5, 1921; University of Illinois College of Medicine, Chicago, 1944; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; on the faculty of the University of California School of Medicine; an officer in the medical corps of the Army of the United States from 1945 to 1947; served an internship and residency at the Cook County Hospital in Chicago; served a residency at the Municipal Contagious Disease Hospital, in Chicago, and the Langley Porter Clinic Hospital, where he was a member of the staff; died in the Palo Alto (Calif.) Hospital July 18, aged 37.

Horton, Ray Beaman ⊗ North Kansas City, Mo.; Kansas City (Mo.) College of Medicine and Surgery, 1922; Magyar Királyi Pázmány Petrus Tudományegyetem Orvosi Fakultasa, Budapest, Hungary, 1924; assistant to the president of the Kansas City Southern Lines; died July 19, aged 58.

Irwin, Henderson, Eureka, N. C.; University of Maryland School of Medicine, Baltimore, 1912; member of the Medical Society of the State of North Carolina and the American Academy of General Practice; for many years chairman of the board of education of Eureka; died in the Woodard–Herring Hospital, Wilson, July 19, aged 74, of carcinoma of the prostate.

Johnston, Cecil Fredrick ⊗ Bluefield, W. Va.; Medical College of Virginia, Richmond, 1929; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; associated with the Bluefield Sanitarium; died July 21, aged 54, of coronary occlusion.

Levant, Benjamin ⊗ Pittsburgh; University of Pittsburgh School of Medicine, 1921; specialist certified by the American Board of Urology; member of the American Urological Association and past-president of the Mid-Atlantic Section; fellow of the American College of Surgeons and the International College of Surgeons; instructor in urology at the University of Pittsburgh School of Medicine; associated with Montefiore Hospital, where he died July 28, aged 60, of coronary disease.

Logan, George W. ⊗ Hastings, Mich.; Saginaw Valley Medical College, Saginaw, 1901; served on the staffs of the Hurley, McLaren General, and St. Joseph hospitals in Flint; died in Flint July 16, aged 81, of arteriosclerosis.

Lombardo, Bartlo William ⊗ Newark, N. J.; New York Medical College, Flower and Fifth Avenue Hospitals, New York City, 1941; certified by the National Board of Medical Examiners; veteran of World War II; associated with St. James and Columbus hospitals, and the Clara Maass Hospital, where he died July 13, aged 41, of cancer.

Lyle, James McCampbell ⊗ Lewiston, Idaho; University of Nashville (Tenn.) Medical Department, 1901; veteran of World War I; medical examiner for the Nez Perce County Selective Service during World War II; on the staff of St. Joseph's Hospital;

served as county health officer and health officer for the city; died in the Gritman Memorial Hospital, Moscow, July 11, aged 81, of pneumonia.

Manglesdorf, William F., Little Rock, Ark.; College of Physicians and Surgeons, Little Rock, 1910; died July 6, aged 79.

Marble, Ira Albertus, Mason City, Iowa; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1907; died July 4, aged 79, of heart disease.

McNealy, Raymond William ⊗ Chicago; born in Chambersburg, Mo., Aug. 17, 1886; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1910; member of the founders group of the American Board of Surgery; served on the faculty of his alma mater and Northwestern University Medical School; professor of surgery and secretary-treasurer of the Cook County Graduate School of Medicine; member of the board of trustees of the Hektoen Institute for Medical Research of Cook County Hospital, of which he was formerly secretary-treasurer; one of the founders and honorary fellow of the International College of Surgeons and chairman of the United States qualifications board; fellow of the American College of Surgeons; president of the Illinois Surgical Society; past-president of the Chicago Surgical Society; president of the United Research Foundation; member of the board of public health advisors, department of public health, state of Illinois; member of the advisory board of the Chicago Health Department; member of the medical advisory board of the Cancer Research Foundation; member of the Western Surgical Association, Pan-Pacific Surgical Society, Southern Surgical Society, Institute of Medicine of Chicago, Alpha Omega Alpha, Alpha Kappa Kappa, and Phi Kappa Epsilon; veteran of World War I; Commander, Legion of Merit–Juan Pablo Duarte, Dominican Republic; in 1941-1942 trustee of Northwestern University; formerly on the editorial board, *Illinois Medical Journal;* president of the attending staff, Cook County Hospital; consulting surgeon at the Illinois Masonic Hospital, Oak Forest (Ill.) Infirmary, and the Kenner Hospital; in 1924 appointed attending surgeon at St. Luke's Hospital; chairman emeritus, department of surgery, and a member of the senior attending staff, Chicago Wesley Memorial Hospital, where he died July 29, aged 71, of cerebral hemorrhage and cardiovascular disease.

Merritt, Francis Elmer, Akron, Ohio; Ohio State University College of Medicine, Columbus, 1934; member of the Ohio State Medical Association; died in the Barberton Citizens Hospital May 21, aged 48.

Meyer, Joseph Theodore ⊗ Chicago; Chicago College of Medicine and Surgery, 1913; fellow of the American College of Surgeons; veteran of World War I; member of the president's council and formerly on the faculty of Stritch School of Medicine of Loyola University; in 1951 was elected president of its alumni association; served as president of the staff and chief surgeon of St. George Hospital, where he died July 29, aged 72, of cerebral hemorrhage.

Montgomery, Claude William ⊗ Sycamore, Ohio; Ohio Medical University, Columbus, 1900; veteran of World War I; formerly member of the board of education; a director and past-president of the board of directors of the First National Bank of Sycamore; past-president of the Sycamore Telephone Company; staff member of the Mercy Hospital in Tiffin; died in the Wyandot Memorial Hospital, Upper Sandusky, July 7, aged 87, of senility.

Moore, Benjamin B. ⊗ Indianapolis; Indiana University School of Medicine, Indianapolis, 1920; fellow of the American College of Surgeons; past-president of the Indianapolis Medical Society; associated with Methodist and St. Vincent's hospitals; on the visiting staff, Indianapolis City Hospital; died near Petoskey, Mich., July 13, aged 62.

Murphy, Dennis John ⊗ Washington, D. C.; Tufts College Medical School, Boston, 1910; service member of the American Medical Association; formerly on the staffs of the Veterans Administration hospitals in Marion, Ind., and Chillicothe, Ohio; veteran of World Wars I and II; served as member of the Veterans Administration pension board; died July 20, aged 71.

Newman, Frederick Jacob, New York City; Columbia University College of Physicians and Surgeons, New York City, 1903; an associate member of the American Medical Association; died in Larchmont, N. Y., July 5, aged 78, of coronary disease.

Oakes, Frederick ⊗ Schiller Park, Ill.; Bennett Medical College, Chicago, 1915; associated with West Suburban Hospital, Oak Park, and Westlake Hospital in Melrose Park, where he died July 28, aged 72, of myocardial infarct.

Pace, William Thomas, Gray Court, S. C.; Medical College of South Carolina, Charleston, 1915; member of the South Carolina Medical Association; for many years on the staff of the Laurens County Hospital in Laurens; died July 6, aged 69, of heart disease.

Pagett, Frank Elmer, Oakland, Calif.; Columbia University College of Physicians and Surgeons, New York City, 1896; at one time practiced in Spring Valley, N. Y., and served as health officer of Rockland County; served as chief of staff at Good Samaritan Hospital in Suffern, N. Y.; died in the Peralta Hospital, July 1, aged 85, of uremia.

Peirce, Bradford Hendrick Ⓜ Hanson, Mass.; Harvard Medical School, Boston, 1906; member of the American Trudeau Society; at one time practiced in Cambridge, where he was health officer; veteran of the Spanish–American War and World War I; served as superintendent and director of the Plymouth County Hospital in South Hanson; died in Brockton (Mass.) Hospital July 16, aged 78, of heart disease.

Plummer, John Owen, Raleigh, N. C.; Leonard Medical School, Raleigh, 1904; died in Durham July 4, aged 78, of myocardial infarction.

Pratt, Frederick Haven, Wellesley Hills, Mass.; Harvard Medical School, Boston, 1906; served as professor emeritus of physiology at Boston University School of Medicine; formerly on the faculty of Wellesley (Mass.) College, University of Buffalo, Clark, and Harvard universities; died July 11, aged 84, of complete heart block.

Quigley, James Earle, Edinburg, Ohio; University of Maryland School of Medicine, Baltimore, 1911; died May 13, aged 74.

Rankin, Pressly Robinson Ⓜ Mount Gilead, N. C.; North Carolina Medical College, Charlotte, 1910; for many years president of the Bank of Mount Gilead, member of the school board and president of the Mount Gilead Brick Company; treasurer of the United Mills Corporation; died in the Montgomery Memorial Hospital in Troy July 6, aged 72, of hepatic cirrhosis **arteriosclerosis** with cerebrovascular accident.

Rivers, Thurston Donnell Ⓜ Montgomery, Ala.; Jefferson Medical College of Philadelphia, 1926; member of the American Psychiatric Association; died July 9, aged 60, of coronary occlusion and arteriosclerotic heart disease.

Sako, Wallace Saburo Ⓜ Raceland, La.; born in Hawaii Sept. 2, 1910; University of Minnesota Medical School, Minneapolis, 1936; certified by the National Board of Medical Examiners; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; served on the faculty of the University of Minnesota Medical School, Minneapolis, Louisiana State University School of Medicine in New Orleans, and University of Texas School of Medicine in Galveston; visiting physician at the Charity Hospital in New Orleans; pediatrician at Sako Clinic for Children; consultant in pediatrics, St. Anne's Hospital, Raceland, St. Joseph Hospital, Thibodaux, Terrebonne Parish General Hospital, Houma, and Southern Baptist Hospital in New Orleans; died July 5, aged 47.

Seldon, Frank Gustav Ⓜ Manchester, N. H.; Friedrich–Wilhelms–Universität Medizinische Fakultät, Berlin, Prussia, 1925; member of the American College of Chest Physicians, and past-president of the New England Chapter, and the American Trudeau Society; formerly associated with the New Hampshire State Sanatorium at Glencliff, and medical superintendent of the Edward Sanatorium in Naperville, Ill.; consultant, Notre Dame de Lourdes Hospital; member of the staff of Sacred Heart Hospital, where he died July 6, aged 59, of arteriosclerotic heart disease.

Sell, Frederick William, Rahway, N. J.; University of Cambridge Faculty of Medicine, England, 1894; past-president of the Union County Mosquito Extermination Commission; at one time health officer; formerly bacteriologist for the Rahway Water Commission; specialist certified by the American Board of Radiology; an associate member of the American Medical Association; served in France during World War I; served on the staffs of New Jersey Reformation Hospital and Rahway Hospital; died in the Alexian Brothers Hospital, Elizabeth, July 9, aged 88, of cerebrovascular accident.

Shanahan, William Henry Ⓜ Portland, Maine; University of Vermont College of Medicine, Burlington, 1912; died in the Veterans Administration Hospital, Togus, June 11, aged 72, of bronchogenic carcinoma with metastasis.

Shannon, Charles Edward Ⓜ Chicago; Rush Medical College, Chicago, 1926; specialist certified by the American Board of Surgery; fellow of the International College of Surgeons and American College of Surgeons; member of the Institute of Medicine of Chicago; veteran of World War I; director of the medical bureau of Marshal Field & Company; on the staff of St. Luke's Hospital; died July 18, aged 60, of coronary occlusion.

Shaul, Elmer Bryant Ⓜ Scranton, Pa.; Syracuse University College of Medicine, 1916; veteran of World War I; on the staff of the Hahnemann Hospital; died July 12, aged 71, of a heart attack.

Sicotte, Isaiah Ⓜ Ishpeming, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1907; practiced in Michigamme; served in France during World War I and received the Croix de Guerre from the French government; died in St. Mary's Hospital, Marquette, July 13, aged 79.

Smith, John William Rosser Ⓜ Charlottesville, Va.; University of Virginia Department of Medicine, Charlottesville, 1900; died July 19, aged 82.

Stansbury, Frank R., Cincinnati; Pulte Medical College, Homeopathic, Cincinnati, 1906; on the staff of the Bethesda Hospital; died July 16, aged 78.

Straith, Claire LeRoy Ⓜ Detroit; born in Harrow, Ont., Canada, Aug. 30, 1891; Rush Medical College, Chicago, 1917; also a D.D.S.; specialist certified by

the American Board of Plastic Surgery; member of the American Association of Plastic Surgeons and the American Society of Plastic and Reconstructive Surgery; fellow of the International College of Surgeons and the American College of Surgeons; associated with Straith Memorial, Harper, Children's, Charles Godwin Jennings, Alexander Blain and Florence Crittendon hospitals in Detroit, and the Highland Park (Mich.) General Hospital; died in Glasgow, Scotland, July 13, aged 66.

Straub, Hiram Grant, Minersville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1917; veteran of World War I; died July 4, aged 67.

Strickland, John Thomas ⊗ Birmingham, Ala.; University of Pennsylvania School of Medicine, Philadelphia, 1946; member of the American Academy of General Practice; past-president of the Birmingham Chapter of the Alabama Academy of General Practice; veteran of World War II; died July 2, aged 42, of injuries received in an automobile accident.

Swanson, Ernest Bruce, Minneapolis; University of Minnesota Medical School, Minneapolis, 1956; served an internship and residency at the Pennsylvania Hospital in Philadelphia; captain and flight surgeon from 327th Air Force Dispensary at Truax Field, Madison, Wis.; killed July 14, aged 27, when a small private plane he was flying crashed near Mauston.

Swenson, Andrew Clay ⊗ Waterbury, Conn.; Yale University School of Medicine, New Haven, 1902; formerly medical examiner of Middlebury; for many years treasurer of the Waterbury Medical Association; on the honorary staff in urology at the Waterbury Hospital, where he died July 19, aged 87.

Talbot, Clarence Weill ⊗ Spokane, Wash.; University Medical College of Kansas City, Mo., 1906; died in the Deaconess Hospital July 1, aged 74, of general peritonitis following gastrectomy for chronic gastric ulcer.

Thomison, Samuel James Jr., Jarrettsville, Md.; University and Bellevue Hospital Medical College, New York City, 1944; certified by the National Board of Medical Examiners; member of the Medical and Chirurgical Faculty of Maryland; veteran of World War II; died in Baltimore July 16, aged 39, of congestive heart failure.

Trice, Leroy ⊗ Palestine, Texas; University of Texas School of Medicine, Galveston, 1931; fellow of the American College of Surgeons; served as secretary-treasurer of the Anderson–Houston–Leon Counties Medical Society; died in the Memorial Hospital, Houston, July 7, aged 51, of hypertensive cardiovascular renal disease.

Vogel, Hymen Allen ⊗ Garden City, Mich.; University of Michigan Medical School, Ann Arbor, 1926; member of the American Academy of General Practice; served as president of the school board; on the staffs of Providence and Mount Carmel hospitals in Detroit, Oakwood Hospital in Dearborn, and Annapolis Hospital in Wayne; died July 2, aged 57, of coronary thrombosis.

Wheeler, David Riddell ⊗ Evanston, Ill.; University of Minnesota Medical School, Minneapolis, 1941; member of the American Psychiatric Association; died July 7, aged 49, of coronary occlusion.

Wheelihan, Robert York ⊗ Riviera Beach, Fla.; Northwestern University Medical School, Chicago, 1928; member of the American Academy of General Practice; served as secretary of the Palm Beach County Medical Society; vice-president of St. Mary's Hospital in West Palm Beach; for many years practiced in Elm Grove, Wis.; formerly health officer for the townships of Brookfield and New Berlin in Wisconsin; died June 25, aged 54, of cancer.

White, William Henry, Banner, Ark. (licensed in Arkansas in 1904); died July 5, aged 77.

Whitehead, Seba L. ⊗ Asheville, N. C.; Jefferson Medical College of Philadelphia, 1921; member of the American Academy of Dermatology and Syphilology; veteran of World War I; associated with Memorial Mission, St. Joseph's, and Aston Park hospitals; died July 12, aged 62, of a heart attack.

Wilkinson, Ernest A., Highmore, S. D.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1905; an associate member of the American Medical Association; died June 1, aged 81, of injuries received in an automobile accident.

Williams, Napoleon Kassire ⊗ McCurtain, Okla.; St. Louis College of Physicians and Surgeons, 1918; member of the school board; on the staff of the LeFlore County Memorial Hospital in Poteau; died July 14, aged 67, of a heart attack.

Woolridge, John Hayes ⊗ Clearfield, Pa.; Jefferson Medical College of Philadelphia, 1916; member of the American Urological Association; fellow of the American College of Surgeons; past-president of the Clearfield County Medical Society; veteran of World War I; served on the staff of the Clearfield Hospital, where he died July 4, aged 67, of coronary thrombosis.

Zanger, Carl Emil ⊗ Chicago; Northwestern University Medical School, Chicago, 1920; veteran of World War I; died July 17, aged 63, of coronary thrombosis.

FOREIGN LETTERS

DENMARK

Antimalarial Drugs for Arthritis.—In four articles in *Ugeskrift for læger* for June 19, Dr. F. Erlendsson reported on the action of various antimalarial drugs on rheumatoid arthritis. The first dealt with 14 patients to whom quinacrine or chloroquine was given, this treatment having been started more than four years earlier. Good results could be claimed in eight. Some of the disappointments in the other patients were due to such side-effects as indigestion and a rash. The second article concerned 20 patients with active rheumatoid arthritis given chloroquine diphosphate whose dose corresponded to 300 to 450 mg. of chloroquine base daily. As a rule the maintenance dose was 150 to 300 mg. daily. The results were satisfactory in 16. The third article dealt with six patients with active rheumatoid arthritis treated with a combination of primaquine and chloroquine. In five the side-effects necessitated a reduction or complete withdrawal of the drugs. The fourth article dealt with the evaluation of therapeutic measures by controlled statistics. Erlendsson preferred the study of the individual patient because of the multiplicity of unknown elements in rheumatoid arthritis.

Old Age and Work.—Dr. Mogens Felbo published a thesis entitled "Old Age and Work." It deals with the relation between the condition of the limbs and capacity for work in 65-year-old and 70-year-old natives of the Danish island of Bornholm. The 974 persons of both sexes belonging to these two age groups submitted to a searching medical examination which showed that loss of muscle strength was more common in laborers engaged in heavy work than in others, that the former suffered more from reduced mobility of the joints, and that while 17.3% of the men had some deformity of the feet, this was the case with 44% of the women. Ulcus cruris was found in 6%, the incidence in women being twice that in men. Arteriosclerosis of the femoral artery was found in 23% of the 65-year-old and in 35% of the 70-year-old men, the corresponding figures for women being much smaller.

Orphenadrine for Parkinsonism.—Dr. P. Berggreen (*Ugeskrift for læger*, June 5, 1958) found orphenadrine to be so effective in treating Parkinsonism that only when it fails is it replaced or given with some other drug. In his series of 25 patients he gave 3 to 12 tablets of 50 mg. daily. The usual dosage was 5 to 7 tablets daily, and, though 12 tablets were well tolerated, no improvement followed raising the dosage over 8 tablets daily. The side-effects were never so serious as to necessitate withdrawal of the drug, and they consisted of dryness of the mouth in 19 patients, blurred vision in 3, smarting of the eyes in 4, constipation in 7, and slight dyspepsia in 6. Altogether 16 patients showed varying degrees of improvement, 8 were not improved, and 1 was made worse. Practically all the patients showing improvement preferred this drug to others they had tried. On this drug the patient's general condition usually improves, he becomes more cheerful and more mobile, but there is no improvement in the tremor.

Herniation of the Nucleus Pulposus.—At a meeting of the Danish Society for Rheumatism Research (*Nordisk medicin*, June 12, 1958) more than one series of statistics concerned with the late effects of operations for herniation of the nucleus pulposus were presented. One speaker insisted that the factors determining the final issue were so varied that the subject did not lend itself to statistical analysis. The material presented by Larsen and Kristoffersen concerned 49 patients operated on in 1950 and 1951 and reexamined five years later. Roughly 50% were found to be completely symptom-free, while the rest still had some pain. Several of the former still presented severe, radiologically demonstrable lesions of the lumbar spine. In another series, presented by J. Saugmann-Jensen, 149 patients were examined from one and one-half to three and one-half years after operation. In 118, complete fitness for work had been achieved, 23 were partially fit for work, and 8 were unfit for work or had had to be operated on again. Broadly speaking, the operation takes the top off the pain, but does not necessarily effect a complete cure.

Health Hazards in Antibiotic Factory.—In 1954 many employees of a Danish antibiotics factory, engaged in penicillin crystallization or streptomycin purification, complained of headache, irritation of the eyes and respiratory passages, and rashes which might be traceable to their occupation. This led to the appointment of Dr. B. Heilesen as medical officer of the factory with the task of supervising the health of its employees. He reported (*Ugeskrift for læger*, June 19, 1958) that in the course of three

The items in these letters are contributed by regular correspondents in the various foreign countries.

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years more than half the cases about which he was consulted were dermatological, largely concerned with streptomycin sensitivity and with penicillin sensitivity, 35 and 10 cases respectively. The reactions were usually eczematous, but in eight of those with streptomycin allergy the reaction took the form of asthma and vasomotor rhinitis. A woman packer of insulin who suffered from urticaria, vasomotor rhinitis, and asthma was cured of these reactions when she ceased work but relapsed on returning to it. Streptomycin was being packed in the same room, and the breaking of ampules containing it was presumably responsible for her symptoms. Heilesen's recommendations are largely prophylactic—the questioning of prospective employees for the most hazardous areas with regard to an earlier history of allergy so that they can be dissuaded from exposing themselves to drug allergy, and mechanizing the packing so that there is as little personal contact as possible with the drugs in question.

FRANCE

Treatment of Acute Leukemia.—R. Picard and coworkers (*Presse méd.* **66**:1064, 1958) treated 11 patients who had leukemia (6 acute and 5 chronic) with prednisone. A follow-up for about two years and the addition of 19 further cases have made possible more substantial conclusions than those previously reported. The effects on the temperature and the general condition were spectacular. The osteoarticular pains were relieved except in those with localized foci who on the other hand responded remarkably to local radiotherapy. The effect on the blood picture however could not be easily assessed owing to the fact that blood transfusions were also given. It was, however, possible to effect a definite improvement in the red and white blood cell counts with prednisone alone and even to get a complete normalization of the hemogram. Furthermore, the functional remission was complete, thus affording the patients a feeling of full recovery.

Hypocholesterolergic Drug.—J. L. de Gennes and co-workers (*Presse méd.* **66**:1108, 1958) stated that evaluation of the hypocholesteremic action of any drug requires (1) a strict selection of the types of hypocholesteremia susceptible of being beneficially investigated, (2) the assessment of an adequate stability in the basic cholesteremia and to the previous determination of its gradients in technical and biological fluctuations, and (3) the ruling out of mere chance as the cause of the fall of the cholesteremia. These requirements were met in the study of a new hypocholesteremic agent (6782). The results obtained indicated a hypocholesteremic effect over a short period.

INDIA

Mecamylamine in Hypertension.—Shah and Shah (*Medical Bulletin*, vol. 3, June 1, 1958) stated that mecamylamine hydrochloride was introduced in the therapy of hypertension as a ganglion blocking agent and acts by blocking the transmission of nerve impulses through both sympathetic and parasympathetic ganglia by raising the threshold of ganglion cells to stimulation. The authors gave this drug to 10 patients with hypertension. All were hospitalized till the maintenance dose was adjusted, and then they were followed as outpatients. The initial dose was 2.5 mg. twice a day and was gradually increased every second or third day till the blood pressure was adequately lowered. All of the patients also received 1 mg. of reserpine daily. The average period of hospitalization required for these patients was five to seven days, and the average maintenance dose was found to be 7.5 to 10 mg. a day in three divided doses. The largest dose given was 45 mg. in 24 hours, and even this dose did not produce any toxic effects.

Results were assessed by the degree of fall in blood pressure, and the criterion of success was the blood pressure response in the upright position without undue giddiness; 9 of the 10 patients responded well to this drug, especially as far as the blood pressure in the upright position was concerned. Symptomatic relief was produced in most patients with regression of blood pressure. The average initial systolic pressure was 210 mm. Hg in the flat and 201 mm. Hg in the upright position. The respective diastolic readings were 123 and 117 mm. Hg. After treatment, these values came down to 174 and 159 mm. Hg systolic and 107 and 99 mm. Hg diastolic. Thus the average systolic fall in the recumbent position was 36 mm. Hg and in the upright position 42 mm. Hg, while the diastolic fall in the two positions was 16 and 18 mm. Hg respectively. The response was maximal in the upright position. Toxic effects observed were constipation, distention, diarrhea, dryness of the mouth, blurring of vision, and giddiness, but in no patient were they severe enough to necessitate cessation of treatment. The drug is especially useful for symptomatic treatment of severe and malignant hypertension.

Urinary Excretion of 17-Ketosteroids in Leishmaniasis.—Chatterjee and Sen Gupta estimated the urinary 17-ketosteroid level in 16 patients with visceral leishmaniasis on admission to hospital and again in 11 after completion of treatment (*Journal of the Indian Medical Association*, vol. 31, July 1, 1958). The patients' ages varied between 10 and 57 years. The diagnosis was confirmed in all cases by the presence of Leishmania donovani in bone marrow, spleen, or liver. Complement fixation and aldehyde tests were also positive in all patients. All of them showed anemia and leukopenia. They were judged

as recovered when the fever disappeared, there was gain in weight, the size of spleen was reduced, and the blood findings returned to near normal levels. In all the excretion of urinary 17-ketosteroids was below normal.

Urinary 17-ketosteroid level estimation is a method of assessing the adrenocortical function, but, as about 30% of the total 17-ketosteroids excreted may be accounted for by testicular secretion, the lowered level in leishmaniasis may be due to adrenocortical and/or gonadal hypofunction. Leishmaniasis is associated with a fair degree of malnutrition which was seen in almost all the patients in this series, along with anemia, leukopenia, and low blood pressure. 17-ketosteroids excretion in the urine is diminished in undernourished persons with or without evidences of malnutrition, and this may be one of the factors responsible for its reduced level in leishmaniasis. In two patients in whom the general condition was fair and the anemia slight, the urinary 17-ketosteroid excretion was less depressed than in the others. In the 11 patients, where it was also estimated after recovery, a distinct increase in excretion was noticed, although the values had not returned to normal in all of these.

Tubeless Gastric Analysis.—Chowdhary and Banerjee (*Indian Medical Forum*, vol. 9, May, 1958) stated that the passage of a Ryle's tube for gastric analysis may prove difficult in nervous patients and is likely to cause some discomfort. As an alternative procedure, a tubeless technique for determining the amount of free hydrochloric acid in the stomach with quinine resin is used. This resin, when given orally, reacts with the free hydrochloric acid of the stomach as a result of which quinine is excreted in the urine. This can be extracted and estimated by measuring its fluorescence in ultraviolet light. The amount of urinary quinine thus estimated indicates the amount of free hydrochloric acid in the stomach.

The authors used this method in 10 patients who were also subjected to a fractional test meal and in whom a Ryle's tube was used, and the results were compared. These patients included six with radiologically confirmed peptic ulcer, all of whom had high acid curves on fractional test meal analysis. All these patients also showed a high excretion of urinary quinine, except one. The remaining four patients had no peptic ulcer, and in all these, except one, a fair correlation was observed between the results of the fractional test meal and the urinary quinine estimation. Thus on the whole, in 8 of the 10 patients, the results obtained with tubeless gastric analysis tallied with those of a fractional test meal. To obtain reliable results, the patients were not given any quinine preparations for a week nor any drugs containing aluminum, barium, calcium, magnesium, kaolin, iron, or vitamins for two days prior to the test. The method is useful in detecting hyperacidity and achlorhydria, but it cannot measure the total and the free hydrochloric acid amounts in the stomach.

NEW ZEALAND

Endocrine Carcinogenesis.—Bielschowsky and Horning (*Brit. M. Bull.* 14:106, 1958) reported that in the last decade views on the role of hormones in carcinogenesis have been greatly modified. New hormones have been recognized and isolated and the metabolic transformations of many steroids clarified. Knowledge of the mechanisms regulating the secretion of these agents has been widened with the result that the pituitary is now considered by many to be the servant of the hypothalamus. Chemical carcinogenesis in the liver depends on pituitary and/or adrenal hormones. Hypophysectomy prevents induction of hepatomas by 3′-methyl-4-dimethylaminoazobenzene and by diacetyl aminofluorene which, however, retains its carcinogenic activity for other tissues. The liver of the hypophysectomized rat still binds the azo dye, but signs of liver damage are missing. The usual reaction to it is restored by giving either ACTH or growth hormone. From the point of view of endocrine carcinogenesis, two different types of cancer occur in animals and men. In hormone-dependent tumors the growth of the neoplasm can be temporarily controlled by an alteration of the hormonal environment in which they develop. Dependent growths are often composed of cells that have been stimulated to proliferate because of a hormonal imbalance, but in some instances they can be induced by extrinsic agents such as irradiation, carcinogenic hydrocarbons, or hormones in combination with irradiation.

Hormone-independent or autonomous lesions, such as those which develop in the skin, stomach, and lung, are not under direct endocrine control, nor can their growth or behavior be influenced by any form of endocrine modification. It is conceivable that some malignant growths might be composed of both dependent and autonomous components. This might explain why a hormone-dependent tumor, whose growth had been previously held in check by means of endocrine therapy, will suddenly lose its responsiveness to a particular hormone or combination of hormones and become an uncontrolled autonomous neoplasm. There appears to be little doubt that the techniques so far used for inducing ovarian tumors in rats and mice are caused by an endocrine imbalance that finally results in tumor formation.

It is, however, more difficult to relate the hormonal theory of ovarian tumor induction to those lesions produced by treatment with carcinogenic hydrocarbons alone. A possible explanation might be that the carcinogens produce a state of anestrus

which would probably cause an increase of pituitary gonadotropins, which in turn would stimulate the ovary. Experimenters and clinicians agree that sex hormones of gonadal and adrenal origin play an important part in the development of tumors of the breast, but the role of pituitary factors is less well understood. Knowledge gained by animal experiment has been of direct value in the application of therapeutic measures for the control of hormonal cancer in man. Recurrences of tumor growth after periods of remission after both gonadectomy and adrenalectomy suggest that the anterior pituitary may be capable of stimulating the neoplasms, or it may be that the recurrence of some mammary carcinomas is due to a pituitary hormone or hormones acting in addition to estrogen. The fact that some forms of endocrine cancer can be fully or partly controlled by alterations of the hormonal environment is, to say the least, encouraging.

PORTUGAL

Neurosis and Internal Medicine.—The Portuguese Society of Internal Medicine invited a group of psychiatrists and psychotherapists to define the role played by the psychiatrist, psychotherapist, and internist in the treatment of neuroses. The number of patients with obsessive, conversion, and anxiety neuroses, with repercussion in internal medicine, is so great that it would be impossible to provide specialized psychotherapy for all of them. For this reason it was proposed to indoctrinate the internists in the relatively simple technique of psychotherapy. The suspected neurotic should be sent to the specialist who would establish his diagnosis and indicate the treatment to be used by the internist. In patients with obsessive neurosis, severe hysteria, and anxiety neuroses of long duration the treatment should be left to a psychotherapist. Most neurotics, however, suffer from a superficial reaction which is accessible to a brief psychotherapy. This should be conducted by the internist, after first being outlined by the psychotherapist.

SWEDEN

Cancer of the Penis.—Ekström and Edsmyr (*Nordisk medicin* [June 26] 1958) made a follow-up study of 229 patients with cancer of the penis. In 156 there were no metastases on admission. Patients under the age of 40 had a metastasis rate of 6:10; between the ages of 40 and 70 it was 3:10; and after 70 it was 2:10. The penis was amputated in 194, and local excision was performed on 20. In 15 x-ray treatment alone was given after an exploratory excision. Inguinal evacuation was performed on 105. In 124 of those with no clinical evidence of metastases of the inguinal nodes, fractional treatment was given with teleradium. Of the 194 with an observation period of at least five years, 17 had died of some intercurrent disease, and 112 had originally been free of metastases. Of these, 101 were still without metastases. Of the 177 survivors, 122 were still without metastases. When a small tumor is limited to the prepuce, it would seem that a local excision assures as good a prognosis as amputation of the penis.

Treatment of Psychiatric Patients with Carbutamide.—Dr. Ewert Ljungberg tells in *Svenska läkartidningen* for June 6 how he discovered the treatment of mental ailments with carbutamide when he gave it to his nonogenarian father who was in need of an oral substitute for insulin to combat his glycosuria. While taking a tablet once a day, the father ceased to be troubled by a sense of loneliness and anxiety and by disturbed sleep. This relief from the depression of old age led Ljungberg to give the drug to 19 mildly disturbed geriatric patients. In 11 the beneficial response was prompt and continuous. No effect was observed in three, and in five it lasted only about a month. This effect was regained when the drug was supplemented by treatment with reserpine. Carbutamide was also given to 20 patients suffering from chronic hebephrenic schizophrenia with remarkable improvement in every case. In some respects, but not all, the reaction to the drug corresponded to the reaction expected from insulin shock.

Pyodermia in Runners.—In the past year 12 cross-country runners with pyodermia were treated in a skin hospital in Gothenburg. Of these, five had to be admitted. This circumstance led to the issue of a questionnaire to the participants in the Swedish cross-country event in 1956 in Gothenburg. Replies came from 52 runners who had suffered from the complaint. Widespread though it seems to be, it has not been described in medical literature. Björnberg and Krook (*Nordisk medicin* [June 12] 1958) pointed out that the onset was usually acute, with multiple cutaneous lesions consisting of folliculitis, pustules, and bullae a few days after running. Boils sometimes developed later. Cultures yielded Staphylococcus pyogenes var. aureus in five patients, the same staphylococci with beta-hemolytic streptococci in one, and beta-hemolytic streptococci alone in two. The superficial lesions healed rapidly with local applications of an antibacterial ointment. This disease is so widespread in Sweden that about 260 of 950 cross-country runners questioned said that they had suffered from it. It is confined to the autumn, coinciding in this respect with the peak of morbidity of impetigo contagiosa. Washing the legs in a disinfectant solution before and after running may help to prevent it. The possibility of infection of one runner by another must be kept in mind.

UNITED KINGDOM

Smoking Genotypes.—Sir Ronald Fisher (*Nature* 182:108, 1958) has always contended that there need not be any direct causal effect between cigarette smoking and cancer of the lung but that both characteristics might be largely influenced by a common cause—the individual genotype. His thesis has been that it was within the capacity of human genetics to examine whether the smoking classes to which human beings assign themselves, such as nonsmokers, cigarettes smokers, pipe smokers, and cigar smokers were genotypically differentiated to a demonstrable extent, or whether, on the contrary, they appeared to be genotypically homogeneous, for only on the latter view could causation, either of the disease by the influence of the products of combustion or of the smoking habit by the subconscious irritation of the postulated precancerous conditions be confidently inferred from the association observed. He recorded the findings of Professor F. von Verschuer, of the Institute of Human Genetics of the University of Munster, in an inquiry into the smoking habits of 51 monozygotic and 31 dizygotic male pairs of adult twins. Of the former, 33 pairs were wholly alike qualitatively: 9 pairs both nonsmokers, 22 pairs both cigarette smokers, and 2 pairs both cigar smokers. Twelve pairs, less than 25% of the whole, showed distinct differences, such as a cigarette smoker and a nonsmoker, or a cigar smoker and a cigarette smoker. By contrast, of the dizygotic pairs, only 11 could be classed as wholly alike. Sir Ronald concluded that there could be little doubt that the genotype influenced smoking habits. The genotypically different groups in this regard would be expected to differ in cancer incidence, and their existence helps to explain such oddities as that pipe and cigar smokers should show much less lung cancer than cigarette smokers, while among the latter the practice of inhaling is associated with less rather than with more cancer of the lung.

Chemotherapy in Pulmonary Tuberculosis of Doubtful Activity.—In view of the many patients under observation whose only manifestation of tuberculosis is an abnormality discovered on mass miniature radiography, in 1954 the Research Committee of the Tuberculosis Society of Scotland decided to investigate whether it was worth while treating such patients prophylactically. The committee reported (*Tubercle* 39:129, 1958) on their findings in a trial which included 189 such patients who were divided at random into two groups: a control group, consisting of 94 patients, kept under observation in the usual way, and a test group, consisting of 95 patients, similarly observed but in addition given a minimum of six months' prophylactic chemotherapy. All the patients were in the trial for at least a year, 61% for 18 months, and 29% for two years. Those in both groups continued to lead a normal working life. Those in the test group were also given 5 Gm. of sodium PAS plus 100 mg. of isoniazid, both twice daily. These were combined in cachet form and were prescribed for a minimum of six months, and thereafter at the clinician's discretion.

Radiographically the estimated cumulative deterioration was 12.6% in the control group compared with 8.1% in the treated group, but six of the seven patients showing deterioration in the treated group admitted that they had failed to take their drugs as directed. Nine positive cultures occurred in the observation group, compared with one in the treated group. The latter was in a patient who had failed to take her chemotherapy as directed. Total deteriorations, radiographic and bacteriological, were 17.8% in the observation group and 8.5% in the treated group. Most improvement or deterioration occurred in the first 18 months of observation. It was concluded that it may be worth while to give chemotherapy prophylactically to certain patients who are at greater risk of relapse, in particular, younger patients and those with more extensive disease. Every effort must be made to persuade such patients of the importance of taking his drugs, and it is well to check the urine periodically for the presence of PAS. Untreated patients should be regularly observed, radiographically and bacteriologically, and should be treated if there is any sign of deterioration. Although this sort of trial may assist the physician in making sound decisions, the patient remains an individual with social, medical, and personal problems. In deciding whether to advise chemotherapy all these must be taken into account.

Smoking and Cancer.—According to the annual report of the Tobacco Manufacturers' Standing Committee—a committee set up by the major firms in the British tobacco industry to assist research into questions concerning the relationship between smoking and health—experiments have been carried out in the industry's laboratories to discover substances which might be used to reduce the minute quantities of benzpyrene in cigarette smoke. A large number of compounds of different types have been examined and so far two substances—copper nitrate and platinum diamino-nitrite—have been found, either of which reduces the benzpyrene content of cigarette smoke. The claim that the addition of 4% ammonium sulfamate to the paper could have a similar reducing effect was not substantiated, although it was shown that the addition of relatively large quantities of ammonium sulfamate to the tobacco does reduce the benzyprene content of the smoke. These findings are based entirely on laboratory experiments. If it were shown that the use of such substances were desirable, investigation of their side-effects would have to be made.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Acute Myocardial Infarction in a City Hospital: I. Clinical Review of 264 Cases. M. Malach and B. A. Rosenberg. Am. J. Cardiol. 1:682-693 (June) 1958 [New York].

The authors report on 162 men (61%) and 102 women (39%), between the ages of 32 and 97 years, with myocardial infarction who were admitted to the Kings County Hospital in Brooklyn, N. Y., between July 1, 1954, and June 30, 1955. One hundred eighty-four patients were between the ages of 61 and 85 years, representing a greater number of older patients in this group than in previous reports. One hundred eight (63%) of the 264 patients were Jews and only 3 were Negroes. Sixty-nine patients had a familial history of heart disease, 61 had evidence of a previous myocardial infarct, and 69 had a history of previous diabetes. Thus, previously reported findings of a greater incidence of myocardial infarction in men, Jews, and patients with a familial history of cardiovascular disease, previous evidence of coronary artery disease, or diabetes mellitus were supported. A very low incidence of acute myocardial infarction in Negroes was observed. Painless cardiac infarction was noted in 55 patients (21%). Of 115 patients with normal blood pressure, 61 died, a mortality rate of 53% as compared with 37 (32%) of 114 patients who had hypertension (blood pressure above 150/90 mm. Hg) on admission or at some time during the hospital course. The latter patients thus showed a greater survival rate than those with normal blood pressure or hypotension. The grave prognosis of shock associated with myocardial infarction was confirmed.

Laboratory studies revealed that 70 patients (29.1%) had a hemoglobin level of more than 15 Gm. per 100 cc. on admission, but this elevation was transient. Cardiac rupture occurred in 3 patients who did not receive anticoagulants but were given ascorbic acid. This observation was paradoxical, since the greater survival rate among those patients who were given vitamin C was statistically significant. One hundred twenty-four (47%) of the patients died; 56 died within the first 48 hours of hospitalization, and 68 died more than 48 hours after admission. This high mortality rate was attributed to the age of the patients, the large number of more critically ill patients, lack of private nursing care, a high incidence of congestive failure, prolonged fever, and tachycardia.

Acute Myocardial Infarction in a City Hospital: II. Experience with Anticoagulants. B. A. Rosenberg and M. Malach. Am. J. Cardiol. 2:71-80 (July) 1958 [New York].

There are 3 points of view with regard to the use of anticoagulants in acute myocardial infarction: (1) they should be used routinely; (2) they should be used selectively; and (3) they should not be used at all. Experience with anticoagulants in acute myocardial infarction reported from large municipal hospitals differs somewhat from that of voluntary institutions. This report deals with the use of anticoagulants in patients with acute myocardial infarction discharged from the University medical service (division 2) of Kings County Hospital, Brooklyn, between July 1, 1954, and June 30, 1955, inclusive. Of a total of 264 such patients, 66 received anticoagulants, while 198 did not receive these drugs. Anticoagulants did not improve the survival rate in this series. There was but 1 major hemorrhagic complication, i. e., hemopericardium without myocardial rupture, related to the use of these drugs, and this complication did not contribute to the death of the patient. The authors observed cardiac rupture in 3 patients who did not receive anticoagulants. The incidence of minor hemorrhagic complications, such as hematuria, in the treated group was of the same order as that previously reported by others.

Serum Glutamic Oxalacetic Aminopherase (Transaminase) Text in Myocardial Infarction: Determination with the Calorimetric Method. D. Ciocia and G. Nodari. Gior. clin. med. 39:621-650 (April) 1958 (In Italian) [Bologna, Italy].

Serum glutamic oxalacetic aminopherase (tranaminase) test by the calorimetric method of Frankel-Reitman was performed on 22 patients with cardiac disease. Unequivocal evidence of myocardial infarction was present in 6 patients, equivocal myocardial infarction in 10, and angina

The place of publication of the periodicals appears in brackets preceding each abstract.

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pectoris not related to myocardial infarction in 16. High serum aminopherase level was observed in patients who had unequivocal, as well as in those patients with equivocal, evidence of myocardial infarction, in whom myocardial infarction was subsequently confirmed by other procedures. Serum aminopherase level did not change in patients with angina pectoris which was not associated with a myocardial infarction.

The specific usefulness of the determination of serum aminopherase level consists in its precocity in establishing the presence or the absence of a myocardial infarction. Elevation of serum aminopherase level was already evident at 4 to 6 hours, and it reached the maximum values 14 to 36 hours after the infarction episode took place. The values decreased afterward and fell to normal levels in 4 or 5 days. Change in leukocytosis, speed of erythrocyte sedimentation, fall of arterial pressure, onset of fever, and electrocardiographic signs of myocardial lesion are factors which complete the diagnosis of myocardial infarction, but only after the change in serum aminopherase level had taken place. Serum glutamic oxalacetic aminopherase test in myocardial infarction is of a lesser prognostic value than other clinical procedures.

Aortic Thrombosis. F. Starer and D. Sutton. Brit. M. J. 1:1255-1263 (May 31) 1958 [London].

The authors report on 24 men and 8 women, between the ages of 37 and 78 years, with aortic thrombosis (Leriche's syndrome) who were admitted to St. Mary's Hospital in London during a 4-year period. Intermittent claudication was present in nearly all the 32 patients and was the outstanding symptom. Loss of power in the legs, frequently accompanied by muscle wasting, appeared to be the symptom next in frequency and occurred in about half of the patients. Four men admitted to impotence (failure to maintain an erection caused by failure of adequate blood supply to the corpora cavernosa through the internal pudendal artery), but it may be presumed that the true incidence of impotence was actually higher. Six patients had mitral stenosis and auricular fibrillation; the aortic thrombosis in these patients was apparently a result of more distal emboli causing retrograde clotting into the aorta. The aortic thrombosis in 3 patients may have been related to trauma. In the other 23 patients the aortic thrombosis resulted from atheroma affecting the common iliac arteries and the lower abdominal aorta. Buerger's disease and other forms of "aortitis," which have been cited as responsible by other workers, are considered to be of little importance. The diastolic pressure was below 90 mm. Hg in 18 patients, from 90 to 100 mm. Hg in 8, from 100 to 110 mm. in 4, and above 120 mm. in 2; these findings show that hypertension is not particularly associated with aortic stenosis, but, since an increased blood pressure predisposes to atheroma, it may become one causative factor in aortic thrombosis. Of 5 patients in whom renal arterial stenosis was observed, 2 had normal blood pressure, 1 had mild hypertension, 1 had a blood pressure of 180/110 mm. Hg, and 1 had a blood pressure of 220/120 mm. Hg. In 1 of these patients an erroneous diagnosis of pheochromocytoma was made.

Plain roentgenograms are of little importance in the diagnosis of aortic thrombosis. Aortography is the most useful procedure in making a positive diagnosis, and it was used in all the patients. The 2 constant features, which between them established the diagnosis, were an abruptly ending column of contrast medium, the block lying anywhere between the level of the renal arteries and the aortic bifurcation, and the presence of a collateral circulation. About half of the patients had occlusion well below the level of the renal arteries, and the others had it directly below this level. In 5 patients the aortic thrombus appeared to be extending into one or the other renal artery. In most of the patients the common iliac arteries were occluded, and flow could be seen to start about the iliac bifurcation. In 1 patient thrombosis extended to the commencement of the femoral artery. The diagnosis of aortic thrombosis should be readily suspected on clinical grounds, but differentiation from bilateral iliac thrombosis is not possible without aortography. Complications of aortography were not observed in this series of patients, and the hazards of aortography recorded by other workers are considered to have been mainly due to faulty techniques. It is concluded that aortic thrombosis is neither as rare nor, in most cases, as dangerous to life as was previously thought.

Signs and Symptoms in Chronic Renal Failure: II. Vomiting, Twitching, Haemorrhagic Diathesis, Convulsions, Itching, and Diarrhoea. P. Effersøe. Acta. med. scandinav. 160:417-430 (No. 5) 1958 (In English) [Stockholm].

In the first of 2 papers an account was given of the relationship between the renal function and the degrees of anemia and acidosis in chronic renal disease. The present study, based on the same 41 patients, is concerned with an analysis of some of the other signs and symptoms that may occur in chronic renal disease. Vomiting, twitching, hemorrhagic diathesis, convulsions, itching, and diarrhea were investigated. It was found that the incidence of vomiting, twitching, and hemorrhagic diathesis rises with increasing impairment of the renal function. Convulsions in nearly all cases are almost certainly of either tetanic or hypertensive origin. Occurrence of "uremic convulsions," independently of these 2 factors, is questionable. Diarrhea is often caused by laxatives in ordinary doses, patients with

impaired renal function being sensitive to laxatives. Edema contributes to the development of diarrhea.

Itching subsided in some of the patients, even though the renal function did not improve. The reason for this may be discontinuation of treatment with an itch-provoking drug prior to admission, and partly reduction during the stay in hospital of the amount of urea on the skin. This reduction may be due to improved hygiene in hospital or, perhaps, to a fall in the serum urea concentration on account of a lower protein content in the diet or to rehydration, the concentration of urea in sweat being proportional to that in plasma.

It was observed also that the incidence of vomiting and twitching is independent of the diet, whether it is normal or low in protein, unless bicarbonate is given. Administration of bicarbonate will probably raise the incidence of vomiting on a low-protein diet and the incidence of twitching on either diet. Hypertension has no demonstrable influence on the incidence of vomiting, twitching, or hemorrhagic diathesis, but it has great influence on the occurrence of convulsions. Vomiting, twitching, convulsions, and itching may occur when the renal function is about 10% of normal, whereas hemorrhages and diarrhea (without attendant edema) usually do not occur till the renal function has been impaired to under about 5%. Acidosis, vomiting, twitching, itching, convulsions, hemorrhagic diathesis, and diarrhea do not occur in patients with chronic uremia, if the hemoglobin level is above 75%.

Hyperchloremic Acidosis in Chronic Pyelonephritis. W. Lathem. New England J. Med. **258:**1031-1036 (May 22) 1958 [Boston].

Hyperchloremic acidosis is a characteristic feature of a variety of kidney diseases that have in common impairment of urinary acidification with the excretion of an alkaline urine. These disorders, which include renal tubular acidosis and the Fanconi syndrome, are characterized principally by minimal alterations in glomerular filtration rate, at least in early stages, and by disturbances in renal tubular function that affect not only urinary acidification but also the tubular transport of glucose, phosphate, urate, amino acids, and potassium. The loss of alkali in the urine or, alternatively, the impairment of hydrogen ion secretion by the renal tubules clearly accounts for the metabolic acidosis common to these disorders, but the origin of the associated hyperchloremia has been confusing. It has been suggested that hyperchloremia may develop as serum bicarbonate diminishes in the interests of maintaining isotonicity and electroneutrality of extracellular fluid when the concentration of other ("undetermined") anions does not change. According to this concept, the ultimate concentration of chloride in extracellular fluid in renal acidosis will be conditioned by the concentration of other anions. Thus, in uremia, in which acidosis is attributable to impairment of tubular secretion of hydrogen ions, the serum chloride concentration may remain constant as serum bicarbonate diminishes, owing to impairment of filtration and retention of undetermined anions. Under circumstances in which glomerular function and tubular function are more or less equally impaired, the concentrations of bicarbonate and undetermined anions in extracellular fluid may change in a reciprocal manner, the chloride concentrations remaining unchanged.

Hyperchloremic acidosis is therefore not unique to the "renal tubular" syndromes but might appear in any renal disease under circumstances in which impairment of tubular function and hydrogen ion secretion are disproportionately greater than changes in glomerular function. The author presents the histories of 4 patients with hyperchloremic acidosis, in whom chronic pyelonephritis was associated with the excretion of an acid urine; hyperkalemia was a prominent feature. These changes appeared before or coincident with the development of azotemia and were attributed to disturbances in renal tubular function. Acidosis and hyperkalemia persisted as uremia developed, but as the concentration of undetermined anions increased in extracellular fluid, hyperchloremia tended to diminish. The acid urine and hyperkalemia and the absence of nephrocalcinosis, hypophosphatemia, and osteomalacia were characteristic features that served to distinguish between the hyperchloremic acidosis of chronic pyelonephritis and that of "renal tubular acidosis."

Multiple Myeloma: Clinical Investigation of Proteinic, Hematological and Renal Changes: 1. Proteinic Changes. V. Prato and P. Chiesura. Minerva med. **49:**1562-1572 (April 25) 1958 (In Italian) [Turin, Italy].

Serum and urine specimens of 14 patients with multiple myeloma were tested for the presence of protein by electrophoresis. Paper electrophoresis revealed abnormal serum protein pattern in 12 patients (85.7%) and normal serum protein pattern in 2. Abnormal beta serum component was observed in 3 patients, abnormal gamma component in 8, and abnormal "M" component in 1. Electrophoretic analysis of the urine showed an abnormal protein pattern in 9 patients (65%). The Bence Jones protein test ordinarily shows an abnormal urine protein pattern in less than one-half of the patients with multiple myeloma. Electrophoretic analysis has thus proved to be a more accurate method than the Bence Jones protein test for determining an abnormal urine protein pattern in patients with multiple myeloma. In the opinion of the authors there is no direct correlation between the serum and the

urine protein components in these patients. The combination of the preceding 2 electrophoretic tests, one for serum and the other for the urine protein components, is a very accurate procedure for the diagnosis of multiple myeloma and may be depended on in almost 100% of instances.

Multiple Myeloma: Clinical Investigation of Proteinic, Hematological and Renal Changes: 2. Hemato-Medullary Changes. V. Prato and P. Chiesura. Minerva med. **49**:1572-1580 (April 25) 1958 (In Italian) [Turin, Italy].

Diagnostic values of the peripheral blood and of myeloma cells in the bone marrow were studied in 15 patients with multiple myeloma. Observation of the peripheral blood revealed only a nonspecific decrease of the bone marrow function. Study of the bone marrow in these patients has proved to be a conclusive diagnostic procedure. Myeloma cells of bone marrow, obtained mostly by sternal puncture, were larger in size than normal plasma cells. The largest observed diameter in cells with 1 nucleus was 28 μ. Cells with nuclei of recent formation, with nucleoli and with slightly basophil protoplasm, were found in all patients. Paraploid was a significant diagnostic feature of the disease; cells with 3 or 4 nuclei were found in all but 1 patient. All the patients had anemia, which was normochromic or slightly hyperchromic, and normocytic or slightly macrocytic. A moderate leukocytosis, which was present in the first stage of the disease, developed into leukopenia. Immature cells, mostly of the granulopoietic group, were found in the circulation of 6 patients (40%). Hemorrhage was observed in 5 patients (33%); it was mostly related to the reduction in the number of platelets and to marked capillary fragility. The latter disorder was observed in 7 other patients.

Bleeding Duodenal Ulcer: Treatment with Bio-Flavonoids and Diet: Report on 36 Cases. S. Weiss, J. Weiss and B. Weiss. Am. J. Gastroenterol. **29**: 629-642 (June) 1958 [New York].

The authors report on 36 patients with hemorrhagic duodenal ulcer who were treated during the years 1952-1956 with the permeability factors known as water-soluble citrus bioflavonoids, which control capillary functioning and arrest capillary hemorrhage. In all cases of bleeding duodenal ulcer the bioflavonoid compound was administered orally, 3 to 9 capsules a day in conjunction with an orange-juice-milk-gelatin mixture and Weiss's modified Meulengracht diet. Twenty-two patients had uncomplicated duodenal ulcer, 4 patients had duodenal ulcer with massive bleeding, 3 patients had perforated duodenal ulcer with severe hemorrhage, and 7 patients had duodenal ulcer with gastric erosions accompanied by massive hemorrhage. All the patients responded to the combined treatment with bioflavonoids, diet, and medication. Bleeding was arrested, and the stool was free of blood in from 6 to 8 days, except in 2 cases where traces of blood in the stool were present for 10 and 13 days respectively. The return of the mucous membrane and the duodenal contour to normal took 10 to 20 days according to roentgenographic examinations. The authors' clinical findings suggest that for most cases of peptic ulcer a medical approach, with emphasis on diet and restoration of integrity of the capillary vessels of the mucosa, should be attempted first. In most cases of duodenal ulcer surgery might be avoided in favor of rational medical approach to this disease.

Neuropsychiatric Symptoms in Liver Insufficiency. B. Harvald and M. Bjørneboe. Acta med. scandinav. **160**:373-384 (No. 5) 1958 (In English) [Stockholm].

Liver insufficiency is the final stage of a number of different diseases of the liver. It may also be observed as a transient or recurring episode. The cause of liver insufficiency is most frequently viral hepatitis or cirrhosis of the liver, but toxic liver diseases, eclampsia, and various forms of occlusion of the biliary tract may also lead to liver insufficiency. The clinical picture is characterized by intense icterus in the great majority of cases, pyrexia, ascites and edema, fetor hepaticus, and various neuropsychiatric symptoms. The authors present observations on the neuropsychiatric symptoms of liver insufficiency in 19 patients who were admitted to the medical department of Blegdamshospitalet during the period from January, 1956, to March, 1957. The patients in this series were carefully followed up with regard to the development of neurological and psychic phenomena; electroencephalograms were recorded in all patients on 1 or more occasions. The material comprises 4 patients with alcoholic cirrhosis, 9 with probable chronic hepatitis, 4 with subacute hepatitis in whom acute hepatitis had developed directly into liver insufficiency, and, finally, 2 with chronic hepatitis in whom portacaval anastomosis had been performed on account of increased pressure in the portal area and subsequent formation of varices and ascites. The majority of the patients were over 60 years old; only the patients in the group with subacute hepatitis and 1 of the patients with portacaval anastomosis were younger.

The neurological symptoms may be divided into 2 groups, mental changes and abnormal motor activity. The mental changes begin insidiously. The patients become lethargic or excited; they become confused and disorientated in time, place, and personal data; the memory is poor, and simple arithmetical calculations cannot be accomplished. The patients urinate and defecate at unsuitable times and places. This stage is followed by som-

nolence, gradually merging into unconsciousness. The development of these mental changes is more acute in hepatitis and slower in cirrhosis. The mental symptoms may be so pronounced that the patient is hospitalized as for psychiatric treatment. The triad consisting of psychic changes, the singular spasmodic movements known as "flapping," and an abnormal electroencephalogram occurs with great frequency. Six of the 19 patients died during the period of observation. Hepatic coma is not a hopeless condition but is, particularly in chronic liver diseases, to a certain extent amenable to therapy and prophylaxis.

SURGERY

Mesenteric Vascular Thrombosis. R. W. Robertson and W. B. Haley. J. Kentucky M. A. **56**:568-571 (June) 1958 [Louisville].

Seven patients with mesenteric vascular thrombosis, ranging in age from 30 to 78 years, were operated on; 6 survived surgery, the 1 fatality being a 78-year-old cardiovascular patient in whom resection was impossible. Five of the 6 survivors contacted recently report that they are in good health and are leading normal productive lives. Although the prognosis is a function of the amount of intestine involved, the age of the patient, the associated conditions, the time lag between onset and surgery, and the preoperative and postoperative care, the decrease in mortality in recent years is due to the strict regulation of electrolyte balance, freer use of blood, and the much improved postoperative care. Supportive therapy in the disease entity, described as recently as 1942 as universally fatal, is particularly important, requiring constant and diligent attention to the patient who has endured resection of sufficient magnitude to be comparable to a severe internal hemorrhage.

Anemia After Subtotal Gastrectomy. J. Van Geertruyden. Acta clin. belg. **12**:171-201 (March-April) 1958 (In French) [Brussels].

In a series of 659 patients followed up from 1 to 10 years after a subtotal gastrectomy for ulcer, cancer, tumor of connective tissue, or polyp, anemia appeared in 17% of the patients. The mean hemoglobin values were 14.1 Gm. per 100 cc. for men and 12.5 Gm. per 100 cc. for women, or about 2 Gm. lower than the values observed in a normal population. Anemia was hypochromic in 15% of the patients and megaloblastic in 2%. Hypochromic anemia is due to several factors: 1. The role of gastric achlorhydria is of little importance. One hundred thirty-five achlorhydric patients had a mean hemoglobin value of 13.1 Gm. per 100 cc.; 23% were anemic. Seventy-four chlorhydric patients had a mean hemoglobin value of 13.7 Gm. per 100 cc.; 14% were anemic. 2. A postoperative protein deficiency reduces simultaneously the hemoglobin and serum albumin levels. In 122 patients studied, a positive correlation was observed between hemoglobin and serum protein and albumin values. 3. With regard to the preoperative hemoglobin level, it was found that patients predisposed to anemia before gastric resection show the same tendency after the operation. 4. Study of the postoperative hemoglobin level showed that anemia is much more frequent in patients in whom this level is low. After subtotal gastrectomy the first 3 factors interfere with the normal hemoglobin synthesis. It is therefore important that all blood deficiencies occurring before and during surgery be perfectly corrected.

The few cases (14) of megaloblastic anemia encountered in patients in the series who had undergone partial gastrectomy were not a consequence of the gastric resection. Most of them were seen in patients operated on for cancer (6 patients or 4.1%) or polyp (7 patients or 35.0%); in these patients the disease was already present before the gastrectomy. One very rare case of megaloblastic anemia (1 patient or 0.2%) appeared after resection for peptic ulcer. Since this (0.2%) frequency is identical with the percentage observed in a normal population, it must be concluded that its appearance is a pure coincidence.

Retrograde Surgical Drainage of Pancreas for Chronic Relapsing Pancreatitis. C. B. Puestow and W. J. Gillesby. A. M. A. Arch. Surg. **76**:898-907 (June) 1958 [Chicago].

In primary pancreatitis, as found in the chronic alcoholic patient, the disease is in the pancreas proper, and operations on the biliary tract or on the head of the pancreas are unlikely to afford relief. There are 5 basic principles which must be understood in arriving at the proper management of this disease entity: 1. The pain of chronic relapsing pancreatitis is due to increased intraductal pressure resulting from partial duct obstruction. 2. Calcification in the pancreas is due to calcium-soap formation in the pancreatic substance, not calcium formation in the duct. 3. The obstruction in the pancreatic duct may be in several places; there is an alternate dilation and stenosis, "chain-of-lakes" appearance, of the duct. 4. Catarrhal inflammation of the duct system occurs wherever strictures are present and prevents free communication of fluid from one dilated area to another. 5. With adequate drainage of the pancreas there is pancreatic regeneration of some degree, and even a severely "burned-out" pancreas may partially recover.

The pain of chronic relapsing pancreatitis will be relieved if and when the ductal system is adequately decompressed, and not, as previously

stated, upon termination of perineural inflammation. Calcification occurs in the substance of the pancreas and is not limited to the pancreatic duct. If the necrosis of the pancreas is adjacent to the duct, the calcification will occur at this site and may involve the duct; however, pancreatic calcifications are not calculi in the sense in which gallbladder and renal calculi are so considered. The contention that the pancreas has the powers of regeneration is valid, and the pancreas is further credited with the ability to recover even when fibrosed or "burned out."

In 1911 Link reported the establishment of an external pancreatic fistula by mobilizing the tail of the pancreas and bringing it to the anterior abdominal wall. Hunt is reported as using retrograde pancreaticojejunostomy in his resections for pancreatic carcinoma. An analysis of the results of the 21 cases in which the modified caudal pancreaticojejunostomy has been carried out by various methods reveals no operative mortality. Two patients died later, and 2 others had recurrence of pain. To the last 4 cases in which the procedure was considered adequate—complete opening and exposure of the pancreatic duct and pancreaticojejunostomy, either by the sheath method or by the side-to-side method—the results have been excellent. The recovery time of this procedure, so far as pain is concerned, is almost immediate. In either method of pancreaticojejunostomy, a Roux-Y reconstruction of the gastrointestinal tract is performed. Pancreaticogastrostomy has been performed on 2 patients. A decision as to whether this procedure is worthwhile is being withheld at this time pending evaluation of clinical material.

Primary Adenocarcinoma of the Ampulla of Vater. W. de Graffenried Hayden and N. C. Hightower Jr. South. M. J. **51**:730-738 (June) 1958 [Birmingham, Ala.].

Eighteen cases of adenocarcinoma of the ampulla of Vater were observed at the Scott and White Clinic, Temple, Texas, during the period from 1924 to 1956. Two cases were excluded from this study because of insufficient pathological material for microscopic proof of diagnosis. Of the remaining number, 12 were proved by biopsy at the time of operation, and 4 were proved by postmortem examination. The ratio of males to females was 13 to 3. The 16 cases bring the total of reported cases of primary adenocarcinoma of the ampulla of Vater to more than 400. The authors conclude that (1) primary carcinoma of the ampulla of Vater is not a rare condition; (2) it is characteristically a small, slow-growing, late-metastasizing growth, amenable to surgical treatment; and (3) it should merit some consideration in the differential diagnosis of persistent pain of a vague nature in the upper abdomen. Any one, or a combination, of the signs and symptoms coincident with an obstructive type of jaundice may represent the earliest evidence of ampullary carcinoma. In the prejaundice stage, laboratory data are of little diagnostic aid other than for the suggestive nature of finding occult blood in the stool.

If there is evidence at the time of operation that the biliary tree is distended behind an obstruction, careful palpation of the duodenum and thorough exploration of the common bile duct may be done without any proof of diagnosis. The passage of instruments through the ampulla of Vater is important. In 4 patients (in 5, counting the 1 noted at postmortem examination), the ampullary region could be palpated, and the common duct was explored well, but there was no suggestion of a malignant lesion at the ampulla of Vater; the duodenum had to be opened to establish the diagnosis. In 1 patient, even opening the duodenum did not establish the diagnosis until biopsy was performed and the tumor was proved by microscopic examination. Thus, in 9 of the 15 patients tested, probes would pass the growth at the ampulla; in 4, there was some evidence of increased resistance which suggested obstruction. When a malignant lesion of the pancreas can be excluded, it becomes mandatory to open the duodenum, carefully inspect the ampulla of Vater for a growth, and perform a biopsy on the ampulla if no gross evidence of a tumor is found. The coincidence of choledocholithiasis and carcinoma of the ampulla is a most treacherous situation as the calculi represent one source of obstruction. Such a situation may be further complicated by the fact that "long-armed" T-tubes may be passed through the ampulla and further mask the presence of a malignant lesion for several weeks. Against such a possibility, transduodenal exploration of the common bile duct is recommended in patients with choledocholithiasis. There seems to be little disagreement that radical surgical procedures are indicated when the patient is able to withstand a wide resection. This study indicates that, if radical surgical procedures are not performed, some type of "bypass" operation would be preferable to local excision of the cancer.

Perforating Peptic Ulcer in Infants. C. M. Grasveld. Arch. chir. neerl. **10**:81-87 (No. 1) 1958 (In English) [Arnhem, Netherlands].

A 10-month-old boy was hospitalized because of a violent convulsion, with increase in temperature. His mother and sister had had abdominal influenza in the course of the same week. Questioning revealed that there had often been black stools in the past. Two days after the admission, hematemesis began. The child was pale and moaned. The abdomen was distended and tender and showed muscular defense. An intravenous infusion was given to counteract the shock, and a laparatomy

was performed as soon as the condition had slightly improved. The laparotomy liberated free air and large quantities of black fluid. A large perforating ulcer was found in the superoposterior part of the duodenum. The pancreas was sutured partly over the defect. Eighteen months after the operation the child was normal for his age. Appetite and growth were satisfactory, and there was no vomiting. No black stools had been passed. The author cites 2 colleagues who had performed operations for perforating ulcer in infants. The histories of these infants are presented. One was admitted 24 hours after birth, and when the peritoneum was opened, gas escaped. The abdominal cavity contained a considerable quantity of bilious fluid and foam. Exploration revealed free perforation of a fingertip-sized ulcer on the anterior side of the duodenum; this was sutured. This girl was in excellent condition when seen about 5½ years after the operation. The other patient was a 14-month-old boy, in whom a perforating duodenal ulcer was found. A Pólya-Reichel modification of a Billroth 2 gastrectomy was performed. Convalescence was uneventful.

NEUROLOGY & PSYCHIATRY

Psychometabolic Changes in Phenylketonuria Treated with Low-Phenylalanine Diet. H. Meyer, E. T. Mertz, H. E. Stadler and others. A. M. A. Arch. Int. Med. 101:1094-1105 (June) 1958 [Chicago].

The dietary approach to the fully developed state of phenylketonuria is a mandatory step, which while not routinely leading to definite general improvement does lend the patient a sense of well-being and increased motor activity heretofore not accomplished. The 6 children chosen for the experiment (most of whom were blond-haired and blue-eyed with blue sclera) were all severely mentally retarded. Four of the 6 patients had obvious cranial and developmental anomalies; 1 was an active epileptic before the research period began and, with 2 other patients, experienced seizures during the experiment. None of the children were toilet-trained; none could feed or dress himself, though 1 of the children had made some progress in this direction; speech was absent, as was any communication within this group; and all of the patients exhibited many of the chracteristics commonly associated with childhood schizophrenia.

Two problems presented themselves. The first was recognition of the pure phenylketonuric. The second was the problem of irreversibility and at what age the therapeutic effect would be questionable. A general analysis of the data reveals an uneven pattern of development, with some slight improvement in the group receiving the diet and some additional improvement in the control group when they were given the diet. There were no changes in mental development, although there were some very definite changes in the area of functional efficiency. Many of the autistic symptoms either disappeared or were abated in the group given the diet, while there was no noticeable change in this area in the control group. Inasmuch as the phenylketonuric patient is burdened with a number of congenital anomalies which are essentially irreversible, any major change in mentation is unlikely. However, the pattern of social maturation is accelerated, and the patient can be trained to complete developmental tasks.

Epidemiology of Poliomyelitis in Switzerland: I. Statistics on Morbidity and Mortality and on the Immunity Status. M. Schär. Schweiz. med. Wchnschr. 88:515-520 (May 24) 1958 (In German) [Basel, Switzerland].

The author lists in a table statistics on poliomyelitis in Switzerland from 1925 to 1957. Figures on the morbidity (number of cases per 100,000 inhabitants) and on the lethality (number of deaths per 100 cases of sickness) show that the morbidity has been greatly increasing since 1936, whereas the lethality is decreasing. Furthermore, in years when the prevalence of poliomyelitis assumes epidemic proportions the lethality rate is much lower than when the poliomyelitis morbidity is low. A lower lethality rate could be caused by a less virulent organism, by improved therapy of severe forms of the disease, or by the diagnosis and reporting of more atypical and nonparalytic cases of the disease. The author regards the first 2 factors as improbable and believes that in epidemics atypical cases are more often reported than when there is no epidemic. Under such conditions it is impossible to recognize minor epidemic trends of poliomyelitis or to evaluate the effectiveness of an immunization campaign. About 70% of the patients with poliomyelitis were children below 15 years of age. The morbidity was greater in males than in females, with the exception of the age group 20-29.

Commenting on periodic fluctuations in poliomyelitis morbidity, the author says that in densely populated areas epidemics seem to develop every 3 or 4 years, whereas in the less populated ones epidemics seem to occur every 5 to 7 years. Serologic tests performed in several Swiss cantons revealed that a relationship between the incidence of poliomyelitis and the immunity status of the child population exists only within geographically limited areas. Morbidity rates alone do not permit one to draw conclusions about the immunity status of the population. The immunity status of a person depends on his age, on his socioeconomic level, and on the frequency of appearance of poliomyelitis

at the place of residence. Boys show higher morbidity than girls but also more frequent inapparent immunization.

Epidemiology of Poliomyelitis in Switzerland: II. The Results of Vaccination During 1956 and 1957. M. Schär. Schweiz. med. Wchnschr. **88**:521-524 (May 24) 1958 (In German) [Basel, Switzerland].

It is estimated that 90% of the cases of poliomyelitis were reported during the years 1956-1957 to either the Swiss Federal Office of Public Health or the Sickness Insurance Organization. Virological and serologic studies on patients, in whom nonparalytic poliomyelitis had been diagnosed, disclosed that many of these cases were caused by agents other than poliomyelitis viruses. Between October, 1956, and May, 1957, about 42% of the population under 20 years of age received at least 2 vaccinations against poliomyelitis, but only about 5% received a third injection. In the year 1957 the number of cases of paralytic poliomyelitis was reduced by 500 in comparison with 1956. The decrease in incidence of the disease was most marked in children between 5 and 15 years of age but was very little in adults between 20 and 29 years of age. Among the young patients with nonparalytic poliomyelitis, 26% were immunized twice or 3 times, among those with paralytic cases, however, only 11.2%. It may be concluded that about 70 to 75% of the vaccinated persons were protected against the paralytic form of the disease. In 1957, 30 to 35% of the poliomyelitis cases were caused by the type 2 and 50 to 60% by the type 1 virus. In the preceding years about 90% of the poliomyelitis cases were due to the type 1 virus. The author points out that most batches of Salk vaccine are much more effective against the type 2 than against the type 1 poliomyelitis virus. Therefore, vaccination may prove less effective in an epidemic caused chiefly by the type 1 virus.

First Results of Vaccination Against Poliomyelitis in Basel in 1956-1957. E. Berger and A. Hottinger. Schweiz. med. Wchnschr. **88**:524-530 (May 24) 1958 (In German) [Basel, Switzerland].

During the vaccination periods 1956-1957, about 30,000 persons in the city of Basel were vaccinated against poliomyelitis with Salk vaccine. Side-reactions to the vaccine were rare. More than 70% of the children between 2 and 14 years were vaccinated, and among those in the first 6 grades of school between 80 and 99% were vaccinated. The efficacy of vaccination was demonstrated by a general reduction in the incidence of poliomyelitis and particularly by a decrease in the paralytic form in children. The authors feel that the number of cases observed is too small for epidemiologic statistics on the prophylactic values of the Salk vaccine.

It was definitely demonstrated, however, that the vaccination increased the virus neutralizing antibodies in the blood. Either such antibodies appeared in the blood after the vaccinations or, if they had been present before, they were augmented. However, the antibody response was not uniform; in a few persons the antibody content was no higher after than before the series of 3 vaccinations. The degree of inapparent immunization, that is, the basic immunity against poliomyelitis, was investigated before vaccination, and it was found that 15% of the population in Basel had antibodies against the poliomyelitis virus as measured by the complement-fixation reaction. Vaccination with the Salk vaccine led to a definite increase in the basic immunity against the disease. The period of effectiveness of the vaccination can be measured by the determination of the neutralizing antibodies present in the circulating blood. The need for additional vaccinations with Salk vaccine can then be estimated.

Determination of Neutralizing Antibodies Against Poliomyelitis Before and After Vaccination with Salk Vaccine in Infants and Young Children. F. Buser, R. M. Du Pan and A. Mégevand. Schweiz. med. Wchnschr. **88**:531-532 (May 24) 1958 (In German) [Basel, Switzerland].

The serums of 28 infants and children were examined for the presence of neutralizing antibodies before and after vaccination with the Salk vaccine. After 2 vaccinations the result was poor. Only in a very few instances could a rise in the level of the neutralizing antibodies be demonstrated. The result after the third vaccination was somewhat better, especially for the antibodies directed against the type 2 poliomyelitis virus. Contrary to the findings of American investigators, optimal levels of the antibodies directed against the type 1 and the type 3 virus could be achieved only in a few instances. This difference is attributed to the new and stricter regulations in the preparation of the vaccine.

Hydrocortisone and Vitamin B_6 in Treatment of Multiple Sclerosis: Preliminary Clinical Note. F. Reyes Oliveros, A. Sixto and M. Garrido Garrido. Med. clín. **30**:118-119 (Feb.) 1958 (In Spanish) [Barcelona, Spain].

Good results with hydrocortisone in the treatment of multiple sclerosis have been reported in the literature (*Rev. neurol.* **94**:352 [April] 1956). The authors administered hydrocortisone and vitamin B_6 to 8 patients with multiple sclerosis, in whom the disease was not of the rapidly progressive type. Hydrocortisone was given intraspinally in doses of 25 mg. twice a week up to a total of 10 injections in 5 consecutive weeks. The injections were given very slowly, the patients remaining in bed for 24 hours after their administration. Vitamin

B_6 was given intramuscularly in daily doses of 300 mg. for 40 consecutive days. At the end of the treatment all the patients reported a feeling of well-being. Two patients who were in the stage of aggravation of the disease, with paraplegia of 1-month duration, walked 2 months after discontinuation of the treatment. The Babinski sign was absent, there was only moderate spasticity, and the cutaneous-abdominal reflexes remained abolished. In 5 patients dizziness disappeared, spasticity diminished, and the function of the vesical sphincter became normal. No benefit from the treatment was reported by the patient in whom the disease was of long duration and with important stabilized neurological symptoms. The results appeared permanent in the other patients during a follow-up period of 1 year and 8 months. The occurrence of frequent spontaneous regressions in multiple sclerosis makes it difficult to evaluate the effects of the aforementioned treatment. The authors believe that in this disease hydrocortisone and vitamin B_6 favor the occurrence of spontaneous regressions of long standing through the antiallergic and antiinfectious effects of hydrocortisone on the nervous system and through the regulation of the metabolism of the nervous system by vitamin B_6.

PEDIATRICS

Transplacental Passage of the L. E. Factor. F. Mijer and R. N. Olsen. J. Pediat. 52:690-693 (June) 1958 [St. Louis].

The authors report a case of probable placental transmission of the L. E. factor from mother to infant. The mother had established disseminated lupus erythematosus, and L. E. cells were repeatedly demonstrated in the peripheral blood of the baby up to the age of 7 weeks. Follow-up examination in the outpatient department after the 7th week showed negative results. Conclusions from a single case would be premature; however, there is no evidence to suggest a hypersensitivity phenomenon immediately after birth. Serum complement and gamma-globulin levels in the offspring were within normal range.

Glycogen Storage Disease of the Heart: Clinical Observations in Five Infants. S. Friedman and R. Ash. J. Pediat. 52:635-647 (June) 1958 [St. Louis].

The authors report on findings in 3 male and 2 female infants, between the ages of 2 and 7 months, admitted to the Children's Hospital of Philadelphia with glycogen storage disease of the heart and skeletal muscles. The birth weight of each was above 3,000 Gm. (7 lb.) except for 1 premature infant who was a twin. The age at the time of death ranged from 4½ to 8½ months. Symptoms were first recognized at least 1 month prior to admission in 4 of the 5 patients and in 2 instances dated from the neonatal period. The family history in each of the 5 infants presented evidence of a genetic determination of glycogen storage disease of the heart. Because clinical and pathological findings in the 5 cases are similar, only 1 is illustrated. At the time of admission the diagnostic impression was upper respiratory tract infection, possibly associated with pneumonitis. A roentgenogram of the chest showed cardiac enlargement but no evidence of pneumonia or of increased pulmonary vascular markings. Antibiotic therapy was unsuccessful. A specimen of the left gastrocnemius muscle showed focal areas with marked vacuolation of the cytoplasm of the muscle fibers. Muscle weakness and flaccidity developed and progressed. Because there was some enlargement of the liver and respiratory distress, digitalization was attempted, which resulted in gross arrhythmia. The difficulties arising from large amounts of tenacious mucoid material in the nasopharynx became progressively greater. Frequent aspirations of the nasopharynx failed to afford relief, and tracheotomy had to be performed. The patient died at the age of 4½ months, 1 month after admission. Postmortem examination of the heart, liver, and psoas muscle tissues revealed glycogen of normal structure as well as a normal amount of amylo 1-6-glucosidase, the enzyme which splits the 1-6-glucosidase linkages which produce the branched structure of the glycogen molecule.

Death in all cases resulted from aspiration, pulmonary infection, and other pulmonary complications. In no instance was frank congestive heart failure observed. The most striking physical findings noted in these 5 patients were those of the neuromuscular system. Paucity of spontaneous movements, generalized muscle weakness, and diminished deep tendon reflexes were consistently present and progressive in all patients. Palpation of the involved skeletal muscles in several instances revealed them to be of average, or slightly greater than average, size, with a firm, rubbery consistency suggestive of muscles observed in pseudohypertrophic muscular dystrophy. Electrocardiographic tracings showed abnormalities simulating those found in other primary myocardial diseases of infancy. On the basis of T-wave changes alone, glycogen storage disease cannot be differentiated with certainty from other lesions. However, study of the QRS complexes offers some information which is useful in differentiating the various entities in this group. The presence of generalized muscle weakness in glycogen storage disease should permit its differentiation from interstitial myocarditis. Two roentgenograms were available for each of the 5 infants, the earliest film being taken at the age of 2 months and the latest at 7 months. The cardiac silhouette was strikingly similar among the 5 patients. In all instances, the cardiac shadow was moderately enlarged with a rounded or globular

contour in all views, particularly the anteroposterior and the left anterior oblique. The cardiac enlargement in each case was of a diffuse nature with no specific chamber enlargement demonstrable. The diagnosis was best made by carrying out a skeletal muscle biopsy. In each of the 4 cases examined in this way, the muscle fibers showed vacuoles containing material with the staining characteristics of glycogen. Generalized muscle weakness was clinically evident at this time in all 4 cases. The absence of abnormal liver function tests, a normal response to epinephrine, and no response to neostigmine (Prostigmin) bromide were also useful indirect or negative contributions to the diagnosis.

Experiences with Cortisone Treatment in Staphylococcic Pneumonia of Infants and Young Children. I. Bühler, H. Feiler and W. Freislederer. Arch. Kinderh. 157:136-147 (No. 2) 1958 (In German) [Stuttgart, Germany].

Of 47 children with staphylococcic pneumonia, who were treated at the children's clinic of the University of Munich during the 2 years from May, 1955, to May, 1957, 35 received, in addition to the customary antibiotic and general therapy, derivatives of cortisone. Seven of these 35 children received hydrocortisone, 3 cortisone, and the others prednisone. The dosage was adjusted to the age of the patient and the severity of the disease. The authors found that in the case of prednisone the daily dose should not be reduced by more than 2.5 mg. per day. The administration of the cortisone derivative was continued for from 5 to 17 days and in the case of recurrence for from 5 to 20 days. Twenty-four of the children received at the conclusion of treatment, for from 2 to 5 days, long-acting corticotropin. The authors did not gain the impression that the omission of the long-acting corticotropin at the end of the treatment would cause a flare-up of some of the symptoms.

The cortisone derivatives were given only to patients with the severest forms of staphylococcic pneumonia, not to the 12 children who had a milder form. Because of this selective factor and because the cortisone derivatives were not the only medication used, the evaluation of their efficacy is difficult. The death rate was only 9%, which compares favorably with the results published in the world literature. An analysis of the clinical courses indicates that this success may be due to the additional use of the cortisone derivatives. The adrenal cortex hormone seems to exert its favorable effect by counteracting the symptoms of shock and by inhibiting exudation. In the 16 infants, less than 4 months old, who were treated with cortisone derivatives, the results were excellent in 9, good in 4, but largely negative in 3. Of 14 older infants and children, 12 obtained excellent or good results. Corticotropin tolerance tests and analysis by paper chromatography on the corticoid cleavage products in some of the children suggested that the action mechanism of the cortisone derivatives, at least in some of the patients, can be explained as a compensatory effect for adrenocortical dysfunction.

Therapy of Pneumonia with Abscess Formation in Infants (with Particular Consideration of Pseudocysts). G. Bucha. Arch. Kinderh. 157:147-155 (No. 2) 1958 (In German) [Stuttgart, Germany].

Although antibiotics have not proved as effective in suppurative pneumonia of infants as had been expected, about two-thirds of the infants with pneumonia that causes abscesses are now curable. In infants less than 3 months old, with miliary distribution of pulmonary abscesses, the course may be rapidly fatal, as local therapy cannot be employed and systemic treatment with antibiotics may fail, even if the causal organism is sensitive to the antibiotic administered. The most frequent form of abscess resulting from suppurative pneumonia is that which perforates into the pleural cleft and forms a pyothorax or even a pyopneumothorax. Extensive surgery, such as rib resection with open drainage, is now generally dispensed with, and the author also prefers conservative treatment. He recommends daily puncture with cautious removal of the pus and with subsequent instillation of a suspension of an antibiotic (50 to 100 mg. of chlortetracycline [Aureomycin] or tetracycline). This local treatment is so effective that continuous drainage can usually be dispensed with; but, if it should prove necessary, closed drainage is advisable. The author found that, if tension pneumothorax develops, it is usually sufficient to insert a nonsuctioning valve (a rubber tube fitted with a rubber finger-stall or a bicycle valve). Because of the favorable gluing tendency of the internal valve, this valve system can usually be removed within a few days.

The author is particularly concerned with the so-called pseudocysts, which he believes are healed, small abscess cavities that become inflated by their connection with the bronchial tree. As a rule, they require no treatment, because they have a tendency to regress spontaneously. Even when they appear to be stationary for weeks or even months, they will generally regress spontaneously in the course of a year. Only if such pseudocysts develop into a spontaneous pneumothorax as the result of maximal inflation, it becomes necessary to deflate them by the nonsuctioning valve system. This is usually accomplished within a few days. The continuous suction drainage, which has been described by others in the treatment of pseudocysts, is regarded by the author as unnecessary, particularly in infants. He feels that the continuous suction carried on over a period of weeks will exert an unfavorable effect on the internal valve. The prognosis as re-

gards the reinflation of the lung and the regression of the adhesions is very favorable in infants. Of the 67 infants with abscess-forming pneumonia, 27 had pseudocysts and, in addition to this, more or less extensive pleural adhesions. But the general condition of these children was relatively good, and the majority could be discharged for ambulatory treatment. This is a great advantage in view of the present-day tendency of the development of resistant organisms in the hospital environment.

Dried Skimmed Milks and Kwashiorkor. P. J. Pretorius, F. J. P. Retief and S. G. Wiechers. South African M. J. 32:563-565 (May 31) 1958 [Cape Town].

Sixty Bantu infants, admitted to hospital with kwashiorkor, were divided in a random manner into 3 equal groups. During a period of 3 weeks one group was given a roller-dried skimmed milk, another group a spray-dried skimmed milk, and the third group a spray-dried acidified skimmed milk. Initially there was a more rapid rise in the serum albumin content among the patients who received the spray-dried milk than among the remaining patients, but after 3 weeks no significant difference could be detected among the values obtained for the 3 groups. The results, therefore, indicate that roller-dried skimmed milk of high quality which has been properly packed and stored can be as effective in initiating cure as spray-dried skimmed milk either with or without added lactic acid. This finding is of economic importance because drum-drying is cheaper than spray-drying.

PATHOLOGY

A Correlated Histological, Cytological and Cytochemical Study of the Tracheobronchial Tree and Lungs of Mice Exposed to Cigarette Smoke: I. Bronchitis with Atypical Epithelial Changes in Mice Exposed to Cigarette Smoke. C. Leuchtenberger, R. Leuchtenberger and P. F. Doolin. Cancer 11:490-506 (May-June) 1958 [Philadelphia].

The interdependence of cigarette smoking and lung cancer was studied in mice whose tracheobronchial trees were exposed to cigarette smoke with the aid of a specially devised smoking apparatus. The results of correlated histological, cytological, and cytochemical studies of the alterations in the bronchi of these animals made it possible to divide them into 3 groups. The first group consisted of bronchi which did not show significant histological changes. The deoxyribonucleic acid content was normal; and nuclear volumes, tyrosine content, and dry mass were not, or were only slightly, increased. In the second group there was bronchitis with mild proliferative epithelial changes. The deoxyribonucleic acid content was not, or was only slightly, increased; and the nuclear volumes, tyrosine content, and dry mass were frequently increased. In the third group there was bronchitis with marked, often atypical, proliferative changes. Atypical basal-cell hyperplasia, squamous-cell metaplasia, or epithelial dysplasia, in many respects similar to what would be called "carcinoma in situ" in man, were seen. The deoxyribonucleic acid content was increased; and the nuclear volumes, tyrosine content, and dry mass were frequently increased. One or more of these features were occasionally present in different areas of the same bronchus.

The similarity between the epithelial lesions of human cigarette smokers and those of mice exposed to cigarette smoke justifies a cautious optimism as to the validity of the authors' experimental approach. It appears that the exposure of animals to cigarette smoke is a useful tool for the study of the interrelationship of cigarette smoking and cancer, despite the realization that this type of cigarette smoke exposure is different from that in the actual process of cigarette smoking.

Tumors of the Anterior Mediastinum. R. W. O'Gara, R. C. Horn Jr. and H. T. Enterline. Cancer 11:562-590 (May-June) 1958 [Philadelphia].

Of 51 patients, between the ages of 4 months and 80 years, with tumors arising in the anterior mediastinum, who were operated on and whose surgical specimens were studied at the laboratory of surgical pathology of the Hospital of the University of Pennsylvania between 1939 and 1955, 16 had thymomas, 3 had carcinomas of the thymus gland, 4 had non-neoplastic lesions of the thymus gland, 10 had malignant lymphomas, 10 had teratomas and related tumors, and 8 had miscellaneous or unclassified lesions. The thymoma was found to be a distinctive tumor of the anterior mediastinum, composed of variable proportions of lymphocytes and epithelial cells. The patients with encapsulated thymomas had a relatively more benign clinical course than did those with nonencapsulated thymomas. No histopathological characteristics were observed that would distinguish benign from malignant thymomas. Several miscroscopic features proved useful in differentiating thymomas from malignant lymphomas of the anterior mediastinum. These included a characteristic cellular pattern, the spindling of epithelial cells, the presence of characteristic cystic spaces, the relative absence of pleomorphism and fibrosis, and the presence of mature and immature concentric (Hassall's) corpuscles. A distinctive adenomatoid pattern was found in 2 encapsulated and 2 nonencapsulated thymomas.

Clinically, patients with thymomas differed from those with malignant lymphomas. Thymomas occurred in an older age group (average age, 51 years)

and were associated with myasthenia gravis in 3 (19%) of the 16 patients with thymomas, who frequently were otherwise asymptomatic. Patients with thymomas had a longer clinical course than did those with malignant lymphomas. Although less responsive to irradiation therapy than the malignant lymphomas, the thymomas did not metastasize. Of the 10 patients with teratomas, 5 had benign cystic teratomas and 5 had malignant teratomas or related tumors. Three of the tumors in the latter group were growing predominantly as seminomas, and the patients showed long-term survival.

PHYSIOLOGY

Role of the Spleen and Effect of Splenectomy in Sickle Cell Disease. C. C. Sprague and J. C. S. Paterson. Blood 13:569-580 (June) 1958 [New York].

The authors determined the erythrocyte survival time by the radioactive chromium (Cr^{51}) method in the circulation of 21 patients with sickle-cell anemia and of 7 patients with sickle-cell hemoglobin (type C) disease and in the circulation of compatible normal recipients to whom sickle cells were transfused. In patients with sickle-cell anemia and enlargement of the spleen, the average half-life time ($T\frac{1}{2}$) for erythrocytes was found to be 3.7 days. After splenectomy $T\frac{1}{2}$ increased to an average of 11.4 days. In patients with sickle-cell anemia who did not have enlargement of the spleen, the average $T\frac{1}{2}$ was found to be 10 days. In 5 patients an average $T\frac{1}{2}$ of 9.2 days was found, whereas the average $T\frac{1}{2}$ for the same cells in the circulation of normal recipients was 4.4 days. In patients with sickle-cell hemoglobin (type C) disease, the average $T\frac{1}{2}$ was 15.7 days. After splenectomy in 2 patients, $T\frac{1}{2}$ was unchanged in one and increased in the other. The $T\frac{1}{2}$ value was shortened in 2 or 3 cases when these cells were transfused into normal recipients, but the data were insufficient to permit conclusions to be drawn. These data show that the survival time of sickle cells is shortened in the presence of a spleen and lengthened (although still much below normal survival time) after splenectomy. It is not unreasonable to postulate that the rigidity of sickle cells interferes with their passage from the splenic pulp, rendering them even more subject to stagnation and eventually to destruction. In the case of the spleen, which is so constructed that stagnation of blood within its pulp spaces is a normal occurrence, it may be concluded that this organ plays a relatively passive role in sickle-cell anemia, the effect of its presence being to accelerate the hemolytic process. Splenectomy would be expected to effect the removal of a principal organ in which sickle cells tend to stagnate and thereby to effect only a mitigation of the hemolytic process. This concept is compatible with the diminution in the severity of sickle-cell anemia frequently recognized in the adult patient whose spleen has atrophied and in the child after splenectomy. Splenectomy was performed on children in whom the erythrocyte survival time was shortened ($T\frac{1}{2}$ less than 6 days).

PUBLIC HEALTH

A Mass Chest Survey at a Naval Station in the Tropics with Notes on Histoplasmosis. S. P. Scalia. Maryland M. J. 7:241-251 (May) 1958 [Baltimore].

At the U. S. Naval Station Rodman in the Canal Zone, 2,185 chest x-rays were taken on 70-mm. film. Those x-rayed included Naval and Marine officers, enlisted personnel and their dependents, and civilian employees of the Navy, most of whom were Panamanians. Among the 900 military personnel x-rayed, only 10 cases (0.09%) with pathological findings were found. Only 4 cases (1.7%) with pathological findings were found among the 233 dependents filmed. Among the 1,052 civilians filmed, 57 cases (5.4%) of disease were discovered. This latter figure represents 1.8% (19) incidence among U. S. civilians and 3.6% (38) incidence among the Panamanian civilians.

The pathological diagnoses totaled 84, although not 1 active case of tuberculosis was found. Several cases of an inactive nature were discovered, all of which had been studied and treated in the past. Since the chest x-ray program was instituted at this facility, there have been 2 cases of active pulmonary tuberculosis discovered per year per 2,000 films. A recent review of 348,875 photofluorograms at the Bureau of Medicine and Surgery disclosed only 63 (0.018%) cases of active pulmonary tuberculosis. This represents the first time that a chest survey at this activity failed to disclose active tuberculosis, a finding that is perhaps more in accord with the tendency toward a world-wide decrease in the incidence of pulmonary acid-fast disease. The finding of histoplasmosis in Americans only (not a single case being found in an adult Panamanian) is, although surprising, in agreement with the recent findings regarding histoplasmosis at the Gorgas Hospital. This disease entity has assumed an important role in the differential diagnosis of chest lesions, since it can so closely mimic pulmonary tuberculosis and malignancy. It has been shown that histoplasmosis is probably the principal cause of pulmonary calcification, and probably the most important cause, as such calcification is so prevalent. Infection with these organisms is postulated as being mild in that these subclinical asymptomatic infections are responsible for the changes seen on x-ray. The differential diagnosis of a lung tumor, a tuberculoma, and a histoplasmoma must often await surgery before it can be resolved, and such was the case in 2 of the cases described here.

BOOK REVIEWS

Electrocardiographic Analysis. Vol. 1: Biophysical Principles of Electrocardiography. By Robert H. Bayley, M.D., Professor of Internal Medicine, Director of Heart Station, University of Oklahoma School of Medicine and University Hospitals, Oklahoma City. Cloth. $8. Pp. 237, with illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This volume attempts to build the background on which the contour of the clinical electrocardiogram depends. It deliberately neglects the recent work on transmembrane potentials—though mentioning it—and concentrates on the factors that give rise to the surface records. It is based on the excellent work, especially of the Wilson school, on electrical properties in a volume conductor, to which the author has made important contributions. While recognizing the modifications which the work of Frank and Burger, among others, have introduced on the simplified concept of the large homogenous electric volume conductor with a small central source of current generation, the author nevertheless minimizes their influence. His concept of a zero potential electrode has been seriously questioned by some. One wonders, furthermore, how important all the mathematical development may be and whether a verbal or graphic presentation would not have served as well. This would have avoided the tendency to dogmatism which mathematical handling tends to impart to the uninitiated. Perhaps this is inherent in the clinician who turns mathematician. In reading some of the clinical concepts in this volume, the same trend to authoritarianism occurs. These flaws are mentioned because they detract from an otherwise excellent development of the biophysical background of clinical electrocardiography. The book deals with the volume conductor theory applicable to electrocardiographic leads, depolarization of the cardiac fiber and heart mass, properties of vectors, heart hypertrophy and block, infarct of the ventricle and the influence of a broad QRS complex on it, the ventricular gradient and repolarization, primary and secondary T-wave changes, currents of injury, and a summarization of mathematical considerations not otherwise dealt with in the text. There is a profusion of multilead clinical electrocardiograms and illuminating graphs. Careful study of the book builds up a sound concept of the basis of clinical electrocardiography that is missing in many other textbooks. The aim is to make clinical electrocardiograms meaningful, and in this the author succeeds. If there is any complaint, it is in the expanded handling of the subject of the ventricular gradient. This volume cannot be read hastily but requires careful and painstaking study—a study well worth the effort of the reader, whether he be a student or novice in the field, a long established clinical electrocardiographer, or a sophisticate of the electrophysiological background of the subject. A critical study of this volume is a must for anyone desiring to know electrocardiography.

So You Want to Be Psychoanalyzed! By Lucy Freeman. Cloth. $3.50. Pp. 145. Henry Holt & Company, 383 Madison Ave., New York 17; George J. McLeod, Ltd., 73 Bathurst St., Toronto 2B, Canada, 1958.

Almost every physician, regardless of his type of practice, has been asked by a patient, "What is it like to be psychoanalyzed?" Now, at last, the physician can answer his patient's, as well as his own, curiosity with a book that provides unusual insight coupled with readable humor and wit. To offer such a book to one's patients provides as complete and close an excursion through analysis as is possible. The book is divided into three sections, each corresponding to a particular stage of psychoanalysis. The first part, called "I love you, I love you, I love you," describes positive transference where the patient develops a love relationship toward the analyst, a feeling that eventually makes it possible to really love someone else in an enduring, intimate fashion. The second part is called "I hate you, I hate you, I hate you." At this stage negative transference takes over because of the patient's reluctance to face the truth about himself. In the last part, after a summary of life's battles with someone who is not interested solely in "making" or "breaking" the patient, analysis is seen as "the temporary crutch that strengthens you to walk alone." When the patient breaks his childish dependence on his physician-analyst, he has achieved a serenity that could stem from the soul, "out of wisdom born of pain and patience and the belief that the noblest struggle of all is to 'know thyself.'"

Just about any conceivable question concerning the "total" experience of analysis will be found in this book: the use of the couch (which is not a requirement), the number of visits, how long analysis will take, what will be talked about, and the recognition of inward success. The book concludes with a chapter exploding the many myths about analysis along with a flat warning: "Analysis does not guarantee that people turn lovable overnight." The author herself says that psychoanalysis can never be adequately described by words. "Your actions, which sometimes speak far louder than the

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words, convey intangible feelings that elude words but are nonetheless real, just as in the first years of your life you talked with your eyes, the tone of your voice, and the movements of your body, without speaking a word." Despite such a warning, this book does give the physician an opportunity to help his patient, where indicated, to make up his mind to help himself.

Recent Advances in Oto-laryngology. By F. Boyes Korkis, M.B., Ch.B., D.L.O., Surgeon and Dean, Metropolitan Ear, Nose and Throat Hospital, London. With foreword by R. Scott Stevenson, M.D., F.R.C.S. Third edition. Cloth. $12. Pp. 438, with 146 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, 1958.

This new edition appears nine years after the second. In that time there have been many advances in all fields of medicine, and the author has attempted to summarize the most significant ones in otolaryngology. The book is well written, with clear, concise summarization of important contributions to the literature. It makes no pretense to be a textbook or to cover all of the available literature. Adequate references are given at the end of each chapter. Chapters deal with anesthesia in otolaryngology, audiology, acoustic trauma, the deaf infant, aural vertigo, the surgical treatment of otosclerosis, sinus infections, carcinoma of the larynx, surgical advances in the treatment of middle ear suppuration, labyrinthine tests, facial palsy, the functions of the nose, benign nasal polyps, the nasopharynx, poliomyelitis and otolaryngology, pharyngeal diverticulum, the salivary glands, and the management of some esophageal diseases. The author has undertaken a difficult task and has done a concise and thorough job. This book is not merely a review of the literature; it possesses a wholesome degree of authority. It is printed on good paper, the print is clear, and it is attractively bound.

Standard Methods of Clinical Chemistry. Volume II. By American Association of Clinical Chemists. Editor in chief: David Seligson. Cloth. $5.50. Pp. 217, with illustrations. Academic Press, Inc., 111 Fifth Ave., New York 3, 1958.

As is volume 1 of this series, this book is a collection of clinical laboratory test methods developed by various workers in the field. Each monograph is listed as having been submitted by a specific author, and the names of the referees who have "verified" the method in their own laboratories are given. The styles of the individual monographs vary somewhat, but in general each contains (1) an introduction which gives the historical development and use of the method; (2) the principles underlying the chemical reaction used; (3) the reagents used and specific directions for their preparation; (4) a procedure which gives detailed directions for conducting the test; (5) calculation of the results; and (6) results and discussion. The discussion of each method is followed by a list of references on the method and other methods for determining the constituent under consideration. Some of the methods given are simple procedures that are applicable for routine use. Others are more complex and are intended for use as "reference" methods to check the more simple routine procedures for accuracy. The tests for which monographs are included in volume 2 are those for calcium (compleximetric), cephalin-cholesterol flocculation, chloride, cholesterol in serum, total fatty acids in stool, gamma globulin in serum, hemoglobin, free and conjugated 17-hydroxycorticosteroids in plasma, iron in serum, 17-ketosteroids in urine, pancreatitis-lipase, nitrogen by the Kjeldahl method, nonprotein nitrogen, determination of blood pH, alkaline and acid phosphatase, phosphatides in plasma, porphyrins in urine, protein-bound iodine in serum, sodium and potassium by flame photometry, sulfobromophthalein (BSP) in serum, and urobilinogen in urine and feces. In some of the monographs, alternate methods are given. The style of these monographs should make the book useful at several levels of interest. For the clinical technician it provides a manual of methods containing specific and detailed procedures. The informal notes spaced throughout the text give words of caution and the simple modifications possible. The information given in the sections on principles and discussion, as well as the references, should make the book a valuable addition to the library of the clinical chemist and pathologist.

Milestones in Modern Surgery. By Alfred Hurwitz, M.D., Professor of Surgery, State University of New York College of Medicine at New York City, and George A. Degenshein, M.D., Assistant Attending Surgeon, Maimonides Hospital, Brooklyn. With foreword by J. Englebert Dunphy, M.D., Professor of Surgery, Harvard Medical School, Boston. Cloth. $15. Pp. 520, with illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

The authors, in choosing the original contributions that in their judgment constitute the "milestones," adopted the following criteria: the article must represent a significant advance in surgery; it must demonstrate the scientific method; and the principle or method described should still be of current value. Twenty-eight were chosen. Each is preceded by a short biographical sketch and a portrait of the author. The original purpose of this volume was to fill a gap in the resident training program. The authors have accomplished much more, for the volume should also be of interest to the mature surgeon, the general practitioner, the specialists in the various branches of medicine, and, in particular, those interested in the history of medicine. The choice of contributions, keeping in mind that the leading idea was emphasis on the principles of surgery, was a happy one. The volume is rounded out by Milestones on the Horizon, in which the story of the development of the extracorporeal pump and renal homotransplantation is told. The volume is a worthwhile addition to the history of surgery and medicine.

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V.

QUESTIONS AND ANSWERS

SIMPLE CHRONIC ANEMIA

To the Editor:—*Please suggest treatment for a patient whose laboratory test shows red blood cells, 4,050,000 per cubic millimeter; hemoglobin level, 12 Gm. per 100 cc. (normal, 13-16 Gm.); white blood cells, 8,800 per cubic millimeter, with polymorphonuclear cells, 42%, lymphocytes, 48%, and monocytes, 4%. Examination shows no other objective symptoms; the only subjective symptom is slight fatigue on exertion.*

James T. Maxwell, M.D., Omaha, Neb.

Answer.—The data suggest that the patient has a mild normochromic, normocytic anemia of the type designated as simple chronic anemia. This is one of the most frequent of all anemias, resulting from depressed red blood cell formation and often from a somewhat greater than normal rate of red blood cell destruction. The causes are many: chronic infection, renal disease, certain endocrine hypofunctional states, tumors, rheumatoid arthritis, liver disease, and others. Correction of the anemia depends on recognition and successful treatment of the disease to which the anemia is secondary. The anemia will not respond to the administration of iron, vitamin B_{12}, folic acid, or any of the "shot gun" antianemic preparations which, unfortunately, flood the pharmaceutical market. Two other possibilities must be mentioned: 1. The anemia could be primarily hemolytic with fairly good compensation by the marrow. Additional information would be required to eliminate or establish that possibility, i. e., reticulocyte count and plasma bilirubin level. 2. If the patient is a woman, the values quoted may possibly be normal; a small percentage of apparently normal women have red blood cell levels of 4 million per cubic millimeter and hemoglobin values of 12 Gm. per 100 cc. In any event, additional diagnostic studies are necessary. It occasionally is true that the most critical diagnostic evaluation fails to reveal the cause of the complaints or of the mild anemia. Under these circumstances, the patient's confidence should be won enough to permit further observation by the physician. With time, usually the anemia will disappear or its cause will become evident.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

EAR ECZEMA AND PREGNANCY

To the Editor:—*A 35-year-old woman has had severe eczema of the ear canal for about five years. The interesting thing is that this came on during her first pregnancy, which resulted in a girl. It has continued with recurrent severe attacks since then, except for remissions during two pregnancies which resulted in boys. She has recently given birth to another girl, and during this last pregnancy her ear condition became much worse. Does this indicate that she has some hormonal imbalance that may account for the external otitis? Many types of treatment have been used, all with little success. She is a nervous individual, but can this condition be on a neurogenic basis?*

Wells C. Carey, M.D., Eureka, Calif.

Answer.—Hormonal influences in various forms of eczema are well known; these include aggravation during menstruation, improvement or aggravation during pregnancy, and the frequent origin of contact dermatitis during the climacterium. Although this consultant has seen different effects of pregnancies in the same woman, such as aggravation during one and improvement during another, a report has never been seen in which the difference depended on whether the pregnancy resulted in a boy or girl. It is not known what, if any, hormonal imbalance may account for such an occurrence.

EXCLUSION GASTRECTOMY

To the Editor:—*It has long been known that removal of a large portion of the fundus of the stomach, with its acid-bearing glands, is apt to be followed by peptic ulceration, whereas removal of the pylorus protects against ulceration. (There is, however, some recent work which shows that the pyloric region can have some inhibitory effect on gastric secretion.) At times, the surgeon is compelled to leave the pylorus in situ as a blind pouch, the so-called exclusion operation. Because this operation is apt to be followed by peptic ulceration, some surgeons remove the mucous membrane of the pylorus before closing it. Is there any evidence that this procedure is effective in preventing ulcer disease or recurrence?*

M.D., West Virginia.

Answer.—Following the exclusion gastrectomy, regurgitation of food substances and alkaline secretions through the afferent jejunal loop, duodenum,

and eventually through the pylorus into the excluded antrum has been demonstrated both experimentally and in man. The neutral food substances excite the antrum both chemically and mechanically to release gastrin, which in turn stimulates the secretion of acid gastric juice by the gastric remnant. Since the acid does not flow over the antrum mucosa, the normal inhibitory effect on gastrin release is negated. As a result, a hypersecretion of acid gastric juice of humoral origin occurs and is frequently followed by recurrent peptic ulceration. Evidence from the laboratory indicates that both chemical and mechanical stimuli are capable of causing the release of gastrin. With removal of the pyloric antral mucosa, chemical stimulation is abolished. The effect of mechanical stimulation of the antrum is abolished by the application of local anesthetics to the mucosa, which suggests that the intramural nerve tissue of the antrum is important in gastrin release. It has been demonstrated histologically that, when one removes the mucous membrane of the antrum, the submucous plexus (Meissner's plexus) is disrupted and probably destroyed, thus preventing mechanical stimuli from exciting the gastrin mechanism. It is theorized from experimental data that gastrin may arise from the submucous intramural nerve plexus, although conclusive evidence is lacking at present. The incidence of marginal ulcer has been reduced since the adoption of Bancroft's procedure of excising the antrum mucosa when it is necessary to transect the stomach proximal to the pylorus in doing gastrectomy for duodenal ulcer.

THE UNFORGIVABLE SIN

To the Editor:—*The question regarding the unforgivable or unpardonable sin, answered in* The Journal *for March 8, 1958, page 1262, is one frequently encountered. The consultant correctly differentiated between original sin and the unforgivable sin, but his definition of the latter was not correct according to the Bible. The passages referring to the unpardonable sin are found in Matthew 12:22-37, Mark 3:22-30, and Luke 11:14-23. A study of these will reveal what was stated, that it is a sin against the Holy Spirit Himself. But it is not a case of "stifling" or "ignoring" Him until one becomes "amoral, beyond reach, and lost." It is not directly connected with one's conscience. The unpardonable sin is committed when one deliberately and knowingly attributes to the devil that which could only have been the work of the Holy Spirit. It is "the blasphemy against the Holy Spirit" of which the Pharisees were guilty when they said, "This fellow (Jesus) doth not cast out demons, but by Beelzebub the prince of the demons" (Matthew 12:24). They were ascribing to Satan that which was the work of God. A careful reading of the Bible passages given above will make this quite clear. Although this sin can be committed today, it does not seem likely that a person in deep concern of soul over it could have been guilty of it.*

Herbert T. Liefeld, M.D.
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Jamaica 35, N. Y.

The above comment was referred to the consultant who answered the original query, and his reply follows.—Ed.

To the Editor:—*It is true that the remarks about the unforgivable sin are found in connection with the criticism that Jesus had cast out demons through Beelzebub. But it is not credible that the people who said this really believed that Jesus was doing it by the finger of God and yet "deliberately and knowingly" attributed it to the devil. They sincerely believed that he was doing it by the devil, and Jesus saw that they could only make such an assertion by stifling their own perception of God. This is the sin against the Holy Ghost. To know that a thing is from God but to say it is from the devil is just to tell a lie and an inconceivable lie at that. No one would dare say such a thing if he really believed that what he saw was God's action. It is just by ignoring the promptings of God in one's heart that one confuses God and the devil and thus becomes "amoral, beyond reach, and lost." As we all agree, no one with a troubled conscience has committed the unforgivable sin. And anyone with a troubled conscience should consult his minister, priest, or rabbi and dwell on the many offers of forgiveness in the Bible. Or, if the guilt feelings are pathological, he must see a doctor.*

HIATUS HERNIA

To the Editor:—*In* The Journal, *May 3, 1958, page 144, a question was concerned with the mechanism of symptoms similar to those of angina pectoris in patients having a hiatus hernia. The answer should have mentioned the frequent occurrence of hypochromic anemia in this condition, with the reduced oxygen carrying capacity of the blood accounting in some cases for the clinical picture of angina pectoris.*

Raymond Schaus, M.D.
56, grand-rue
Luxembourg, Europe.

The above comment was referred to the consultant who answered the original query, and his reply follows.—Ed.

To the Editor:—*It is true that retrosternal distress due to the reduced oxygen carrying capacity of the blood in hypochromic anemia may be confused with the pain of angina pectoris. However, the chief cause of the difficulty in diagnosis is the pain caused by peptic esophagitis or distention of the intrathoracic portion of the stomach.*